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(54) **RUTHENIUM COMPLEXES AND THEIR USES IN PROCESSES FOR FORMATION AND/OR HYDROGENATION OF ESTERS, AMIDES AND DERIVATIVES THEREOF**

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None
See application file for complete search history.

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(57) **ABSTRACT**

The present invention relates to novel Ruthenium catalysts and related borohydride complexes, and the use of such catalysts, inter alia, for (1) hydrogenation of amides (including polyamides) to alcohols and amines; (2) preparing amides from alcohols with amines (including the preparation of polyamides (e.g., polypeptides) by reacting dialcohols and diamines and/or by polymerization of amino alcohols); (3) hydrogenation of esters to alcohols (including hydrogenation of cyclic esters (lactones) or cyclic di-esters (di-lactones) or polyesters); (4) hydrogenation of organic carbonates (including polycarbonates) to alcohols and hydrogenation of carbamates (including polycarbamates) or urea derivatives to alcohols and amines; (5) dehydrogenative coupling of alcohols to esters; (6) hydrogenation of secondary alcohols to ketones; (7) amidation of esters (i.e., synthesis of amides from esters and amines); (8) acylation of alcohols using esters; (9) coupling of alcohols with water to form carboxylic acids; and (10) dehydrogenation of beta-amino alcohols to form pyrazines. The present invention further relates to the novel uses of certain pyridine Ruthenium catalysts.

21 Claims, 8 Drawing Sheets

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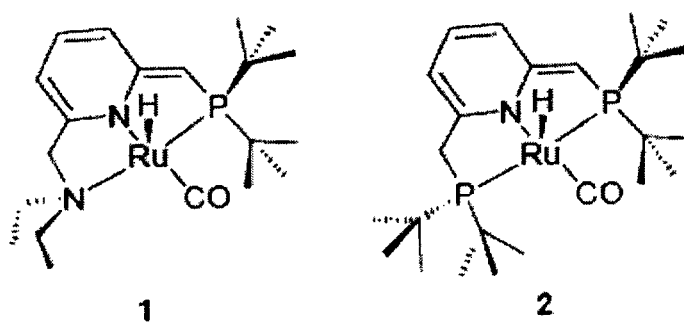
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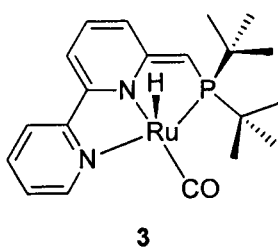
Figure 1B
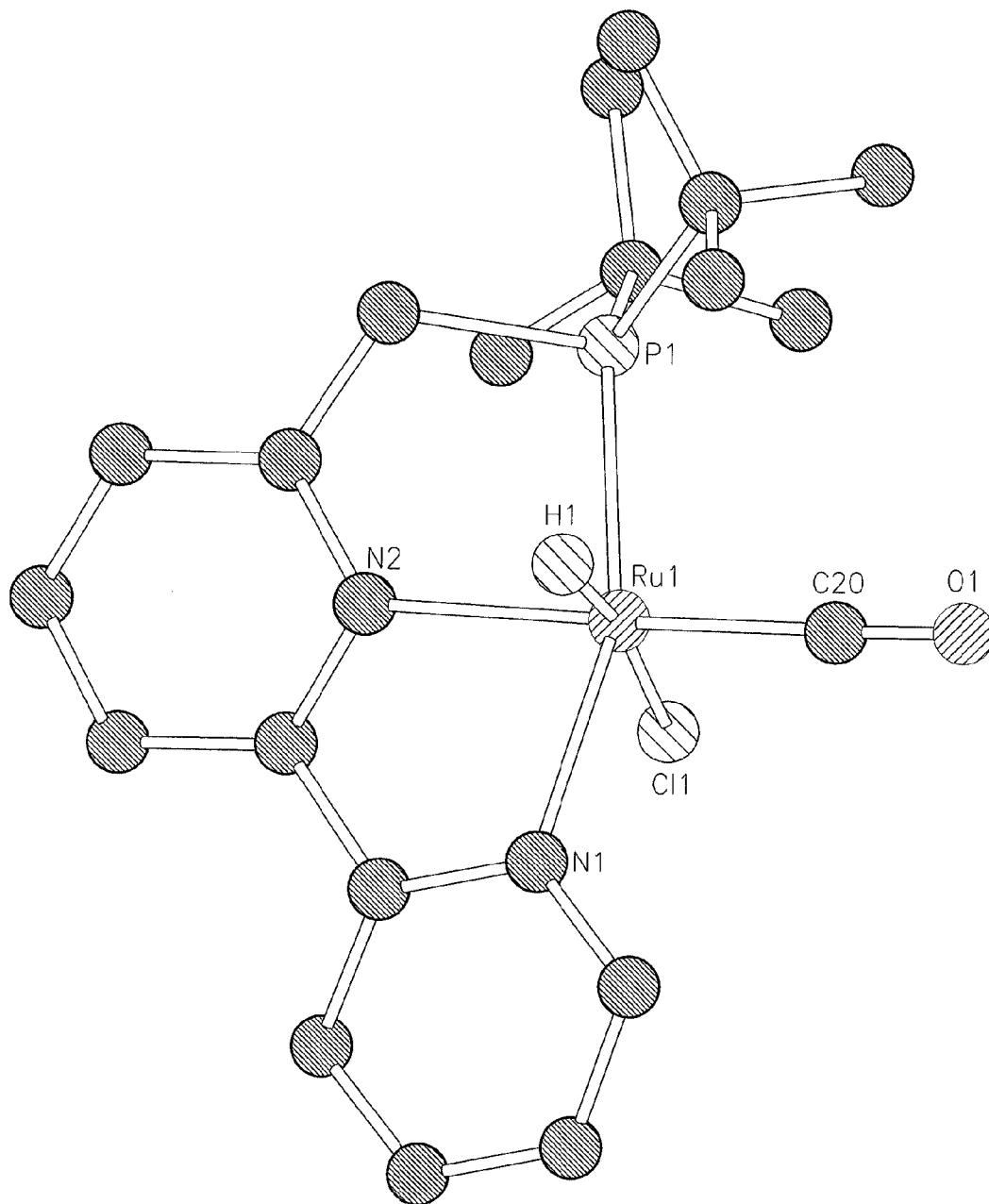
FIG.2
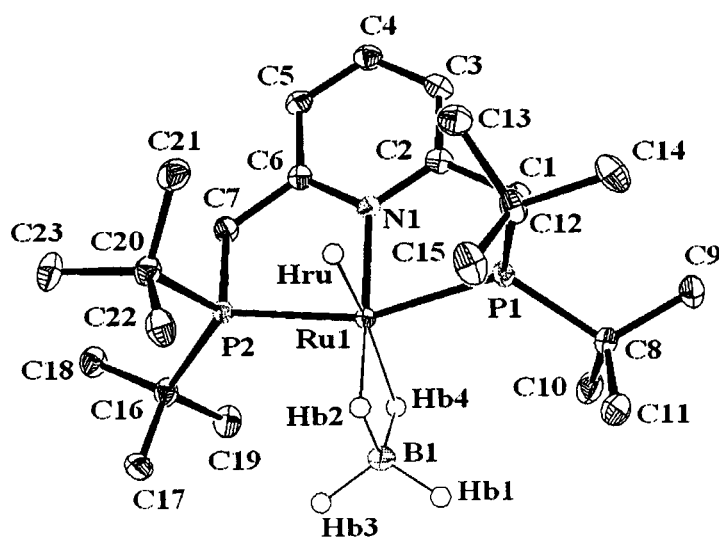
Figure 3

FIG.4

FIG.5A

FIG.5B

842.88
1116.47
1386.51
1661.17
1935.92
2210.17
2484.62
2762.08
3034.56
3309.74
3582.16
3861.94
4144.28
4410.83
4682.13
4974.29
5254.63
5526.62
5783.04
6102.03
6351.74
6641.13
6904.09
7199.01

1000   2000   3000   4000   5000   6000   7000   8000

FIG.5C

1100   1600   2100
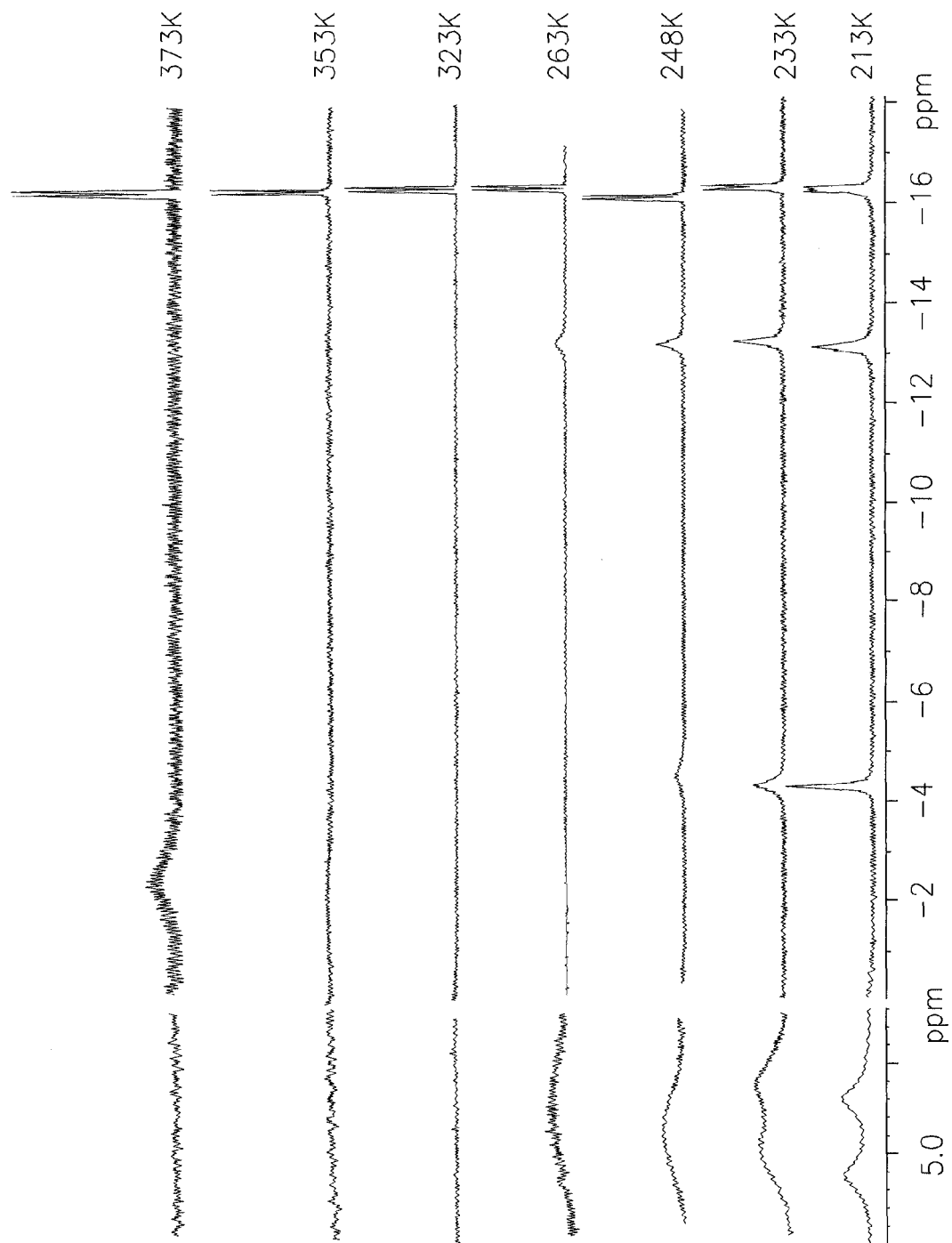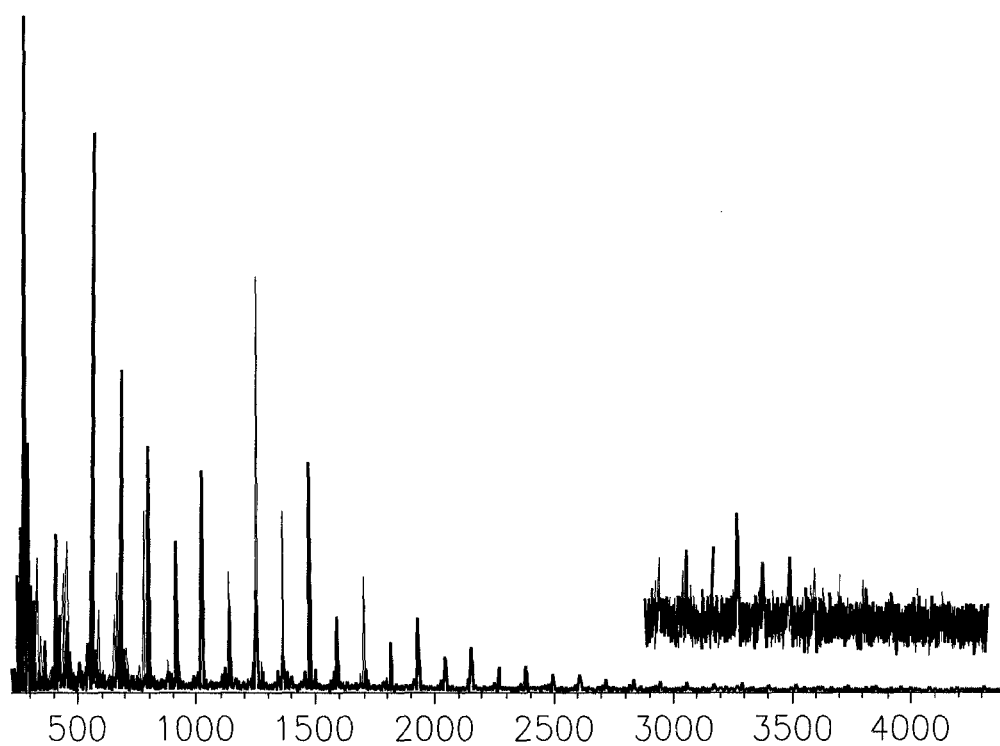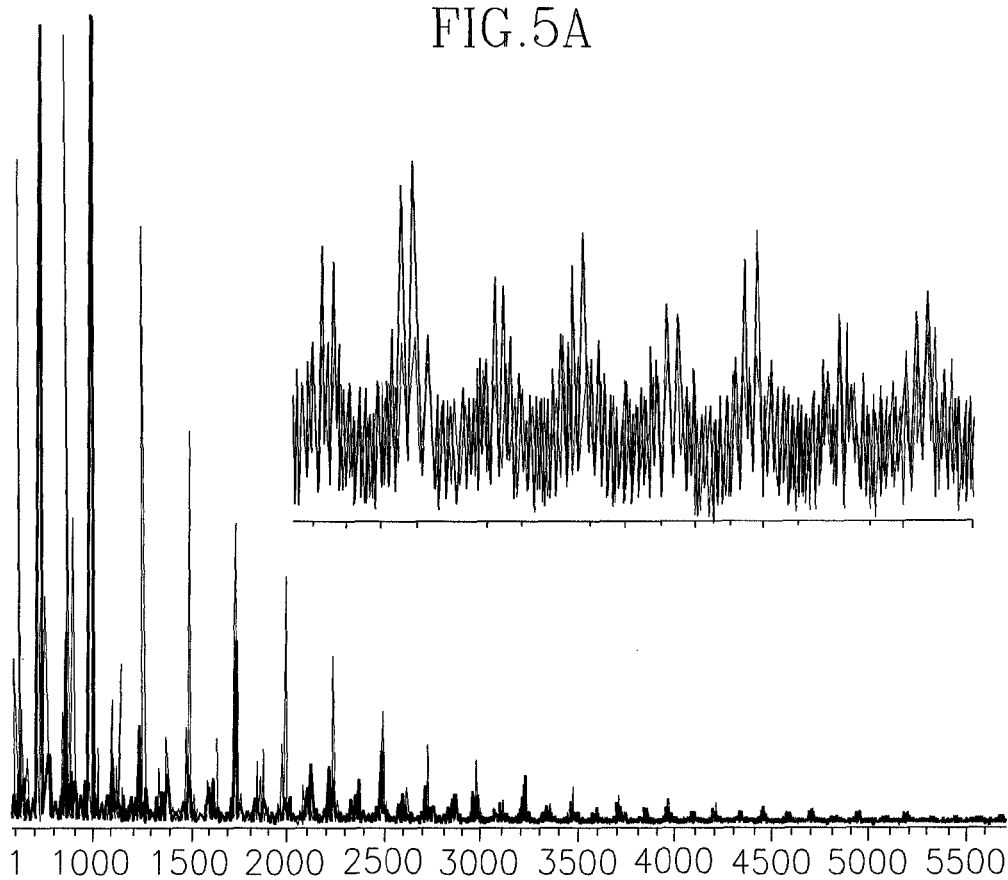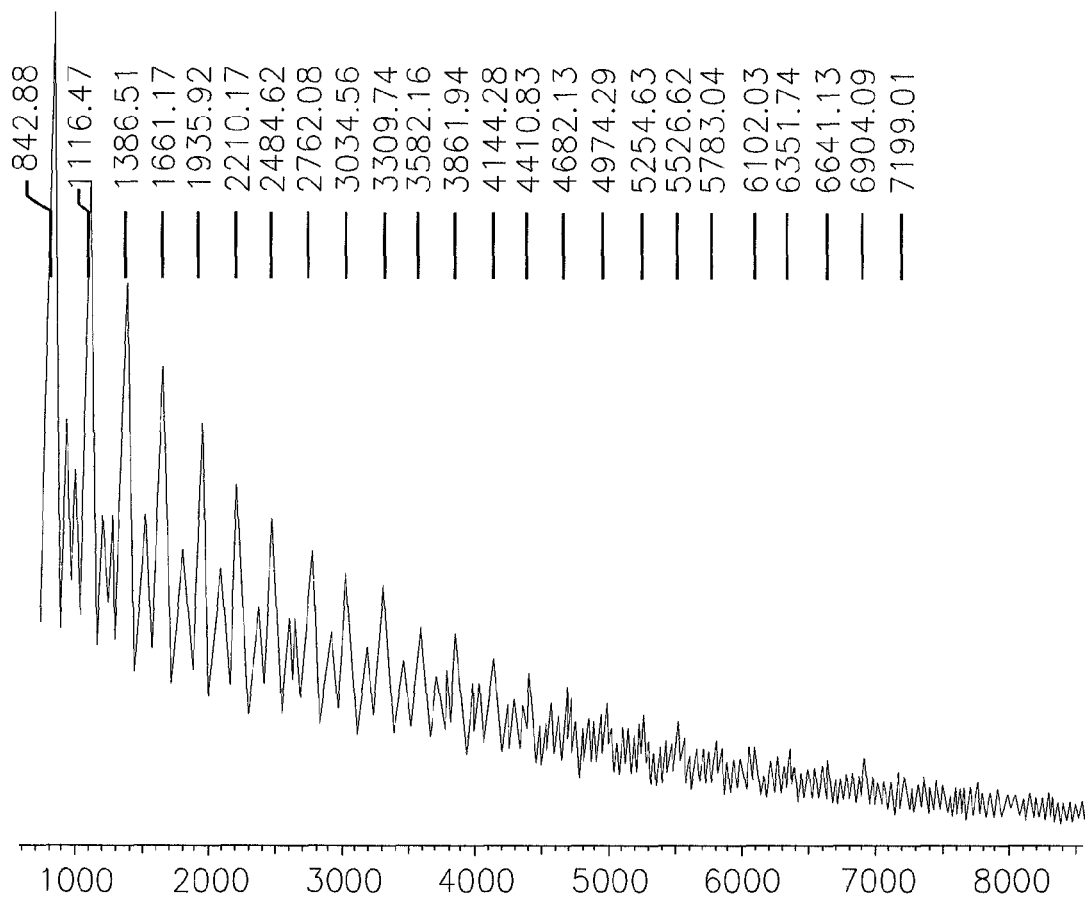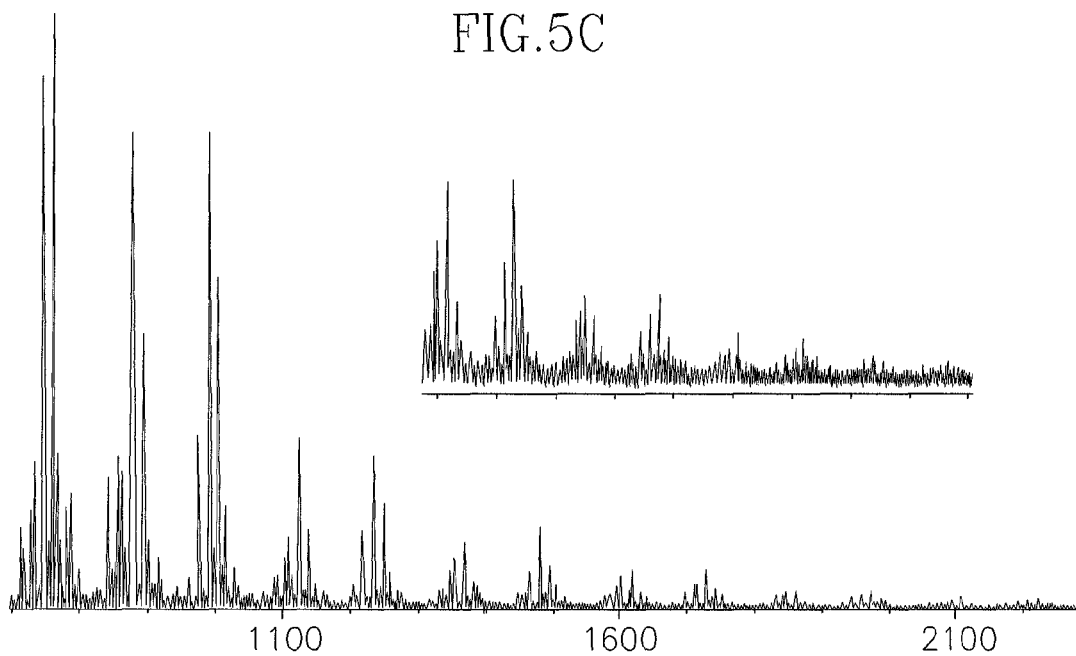
FIG.5D

FIG.5E

Figure 6

# RUTHENIUM COMPLEXES AND THEIR USES IN PROCESSES FOR FORMATION AND/OR HYDROGENATION OF ESTERS, AMIDES AND DERIVATIVES THEREOF

FIELD OF THE INVENTION

The present invention relates to novel Ruthenium complexes and related borohydride complexes, and their use, inter alia, for (1) hydrogenation of amides (including polyamides) to alcohols and amines; (2) preparing amides from alcohols with amines (including the preparation of polyamides (e.g., polypeptides) by reacting dialcohols and diamines and/or by polymerization of amino alcohols); (3) hydrogenation of esters to alcohols (including hydrogenation of cyclic esters (lactones) or cyclic di-esters (di-lactones), or polyesters); (4) hydrogenation of organic carbonates (including polycarbonates) to alcohols and hydrogenation of carbamates (including polycarbamates) or urea derivatives to alcohols and amines; (5) dehydrogenative coupling of alcohols to esters; (6) dehydrogenation of secondary alcohols to ketones; (7) amidation of esters (i.e., synthesis of amides from esters and amines);

On the other hand, selective, direct hydrogenation of amides to form amines and alcohols has not been reported. Hydrogenation of amides to amines (via C—O cleavage, generating water) can have C—N cleavage as a side reaction, requiring the presence of water, and resulting from catalytic hydrolysis of the amides to acids and amines, followed by hydrogenation of the acids to alcohols: see Núñez Magro et al. and Beamson et al) However, no amide C—N hydrogenolysis to form alcohols and amines was reported in absence of water.

Amines and alcohols are used extensively in the chemical, pharmaceutical and agrichemical industries (Lawrence; Ricci; Kumara et al.). Design of such a reaction is conceptually challenging, since the first mechanistic step in amide hydrogenation is expected to be H_2 addition to the carbonyl group to form a very unstable hemiaminal which, in the case of primary or secondary amides, spontaneously liberates water to form an imine; further hydrogenation of the imine then leads to amine formation (Scheme 1). For amine and alcohol formation, cleavage of the C—N bond in preference to the C—O bond is required.

Scheme 1. General scheme for hydrogenation of amides.
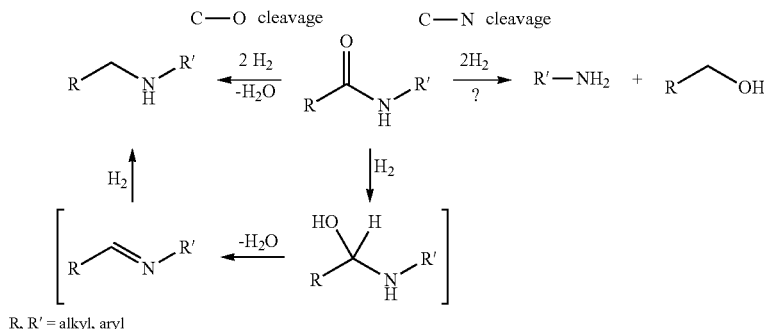
R, R′ = alkyl, aryl

(8) acylation of alcohols using esters; (9) coupling of alcohols with water and a base to form carboxylic acids; and (10) dehydrogenation of beta-amino alcohols to form pyrazines. The present invention further relates to the novel uses of certain pyridine Ruthenium complexes.

BACKGROUND OF THE INVENTION

Reduction of carboxylic acids and their derivatives plays an important role in organic synthesis, both in laboratory and industrial processes. Traditionally, the reduction is performed using stoichiometric amounts of hydride reagents, generating stoichiometric amounts of waste (Seyden-Penne). A much more attractive, atom-economical approach is a catalytic reaction using H_2; however, hydrogenation of carboxylic acid derivatives under mild conditions is a very challenging task (Rylander; Hartwig), with amides presenting the one of the highest challenges among all classes of carbonyl compounds. A few examples of the important hydrogenation of amides to amines, in which the C—O bond is cleaved with the liberation of water (Scheme 1), were reported (Hirosawa et al., Núñez Magro et al., Beamson et al.). This reaction can also be affected with silanes as reducing agents (Fernandes et al., Das et al.). In addition, the interesting hydrogenation of cyclic N-acylcarbamates and N-acylsolfonamides, which involves cleavage of the C—N bond, but does not form amines, was recently reported (Ito et al., 2009).

The reverse reaction, i.e., amide formation from alcohols and amines with liberation of H_2, was previously reported by inventors of the present invention, and later, by others (Nordstrom; Ghosh; Shimizu) Formation of amides from alcohols and amines by use of hydrogen acceptors was also reported recently (Zweifel; Watson). The importance of amides in chemistry and biology is well recognized and has been studied extensively (Sewald et al.; Greenberg et al.; Smith and March; Bray). Although several methods are known for the synthesis of amides, preparation under neutral conditions and without generation of waste is a challenging goal (Larock; Smith). Synthesis of amides is mostly based on activated acid derivatives (acid chlorides, anhydrides) or rearrangement reactions induced by acid or base which often involve toxic chemical waste and tedious work-up (Smith). Transition-metal catalyzed conversion of nitriles into amides was reported (Cobley et al.; Murahashi et al. 1986 and 1992). Catalytic acylation of amines by aldehydes in the presence of a stoichiometric amount of oxidant and a base is known (Tamaru et al., Tillack et al.). Recently, oxidative amide synthesis was achieved from terminal alkynes (Chan et al.). Cu(I) catalyzed reaction of sulfonyl azides with terminal alkynes is a facile method for the synthesis of sulfonyl amides (Cho et al.; Cassidy et al.).

Polyamides are one of the most important polymer classes, extensively used in fiber products, plastics and their deriva-

tives, with many applications, including in biomedical studies. Recently, the synthesis of functional polyamides has received considerable attention. Generally, polyamides are synthesized by condensation of diamines and activated dicarboxylic acid derivatives and/or in the presence of coupling reagents. In some cases, ring opening of small-ring lactams at high temperatures leads to polyamides. To avoid the use of activators, waste generation, or harsh conditions, the development of economical, efficient and environmentally benign protocols are desirable.

Transition metal borohydride complexes display extensive reactivity with organic substrates and are useful starting materials for the preparation of transition metal hydrides and borides (Dick et al; White et al). They have found uses in catalytic hydroboration (Burgess et al., Isagawa et al., Lee et al); polymerization of olefins (Barbier-Baudry et al., Bonnet et al, and Marks et al.) and cyclic esters (Palard et al.). Ruthenium hydrido borohydride complexes based on bidentate phosphorus ligands and diamines, reported by Ohkuma et al, Sandoval et al. and Guo et al. are effective catalysts in asymmetric transfer hydrogenation of ketones (Ohkuma et al., Sandoval et al., Guo et al) and enantioselective Michael addition (Guo et al.). In addition, borohydride complexes may represent plausible models for CH_4 coordination in the transition state for C—H activation (Jensen et al. 1986 and 1988).

Transition metal complexes of bulky, electron-rich tridentate ligands have found useful applications in synthesis, bond activation, and catalysis (see recent reviews: Van der Boom et al., Albrecht et al., Vigalok et al., Jensen 1999 and Rybtchinski et al.). The highly electron-donating ^{t}Bu-PNP (2,6-bis(di-tert-butylphosphinomethyl)pyridine) and its group 8 metal complexes have been explored by several groups (Kawatsura et al., Stambuli et al., Gibson et al., and Kloek et al) as well as by some of the inventors of the present invention (Hermann et al., Ben-Ari et al. 2003 and 2006, Zhang et al. 2004, 2005 and 2006, and Feller et al).

Dehydrogenation of alcohols to carbonyl compounds without a hydrogen acceptor or oxidant, with the evolution of molecular hydrogen, is attractive economically and environmentally (Scheme 2), but homogeneous systems capable of thermally catalyzing dehydrogenation of alcohols are relatively rare (Zhang et al. 2004 and 2005, Murahashi et al. 1987, Charman et al., Morton et al., Dobson et al., Jung et al., Ligthart et al., Shinoda et al., Matsubara et al., Adair et al., Lin et al. 1997 and 1992, Blum et al., and Zhao et al.).

Scheme 2

$$RCH(OH)R' \xrightarrow{\text{Catalyst}} \underset{RCR'}{\overset{O}{\overset{\|}{}}} + H_2$$

$$2\ RCH_2OH \xrightarrow{\text{Catalyst}} RCOOCH_2R + 2H_2$$

(R = alkyl, aryl; R' = alkyl, H)
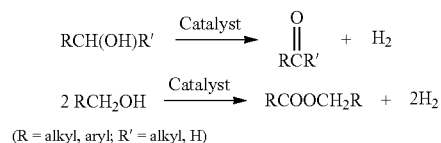
Catalytic hydrogenation of polar carbonyl bonds is a simple, convenient, and sustainable method which plays a pivotal role in both industrial processes and academic research. The hydrogenation of esters to alcohols is an important transformation and remains a challenging task in the perspective of "green and sustainable chemistry (GSC)" where the transformation is atom-economic without generating any large amount of metal waste. Despite well-documented homogeneously catalyzed reductions of ketones and aldehydes, the catalytic hydrogenation of esters to alcohols under mild and homogeneous conditions is relatively under-

developed, owing to the poor hydridophilicity (electrophilicity) of the ester carbonyl functionality. The common trend in the reactivity of carbonyl groups towards hydrogenation reactions is RC(O)H>RC(O) R'>>RC(O)OR'>RC(O)NR'.

Simple 1,2-diols, e.g., propylene glycol (PG) and ethylene glycol (EG), are utilized as high value-added specialty chemical intermediates, in the manufacture of biodegradable polyester fibers, unsaturated polyester resins, antifreeze, pharmaceuticals and other important products. Currently, these two vicinal diols are industrially produced from petroleum-derived propylene and ethylene via hydration of their corresponding epoxy alkanes. However, as crude oil resources become limited, substitutes for petroleum feedstocks are increasingly sought after, and as such the synthesis 1,2-diols, indirectly from biomass derived resources is of great interest. Alternative methods which proceed under mild reaction conditions with stable and easy-to-handle homogeneous catalysts and environmentally benign are desirable.

Glycolide and lactide are important classes of cyclic diesters (di-lactones) utilized as starting materials for Lewis-acid catalyzed polymerization reactions to synthesize biodegradable polymers. Since these compounds are produced from biomass derived resources such as glycolic acid (derived from sugar cane) and lactic acid (from fermentation of glucose) respectively via self-esterification, their efficient hydrogenation can provide alternative, mild approaches to the indirect transformation of biomass to important synthetic building blocks. Although few catalytic hydrogenations of (mono lactones) to diols are known in the literature, the complete hydrogenation of cyclic di-esters to the corresponding 1,2-diols (e.g. ethylene glycol and propylene glycol) is extremely difficult due to presence of two ester moieties and the chelating ability of the final product, 1,2-diol, which may retard the catalytic activity of the catalyst. Indeed, to the applicant's best knowledge, catalytic hydrogenation of these important families of cyclic di-esters has never been reported, be it under heterogeneous or homogeneous catalysis.

The applicants of the present invention have recently reported on new catalytic reactions of alcohols, such as dehydrogenative coupling of primary alcohols to esters and dehydrogenation of secondary alcohols to ketones using pyridine-based pincer complexes (Zhang et al. 2004, 2005, 2006 and 2007; Gunanathan 2007; Gnanaprakasam and Milstein) and acridine (Gunanathan 2008 and 2009). The catalytic efficiency of the reaction of the conversion of primary alcohols to ester was enhanced with Ru(II) complexes of an analogous ligand having a potentially "hemilabile" amine "arm", PNN (2-(di-tert-butylphosphinomethyl)-6-(diethylaminomethyl) pyridine). (PNN)Ru(II) complexes effectively catalyze the acceptorless dehydrogenation of primary alcohols to the corresponding esters and molecular hydrogen in high yields and turnover numbers, in the presence of a catalytic amount of base. Mechanistic studies of this reaction have led to the discovery of a PNN Ru hydrido carbonyl complex, which does not require the presence of base, the catalytic reaction proceeding very effectively under neutral, mild conditions (Zhang et al. 2005).

The pyridine-based PNN Ru complex 1 (FIG. 1A) efficiently catalyzes the dehydrogenative coupling of alcohols to form esters (Zhang 2005, Zhang 2007 and Milstein), the hydrogenation of esters to alcohols under mild conditions (Zhang 2006 and Milstein) and the coupling of alcohols and amines to form amides and H_2 (Gunanathan 2007 and Milstein). The PNP complex 2 (FIG. 1A) is an efficient catalyst for the dehydrogenative coupling of alcohols and amines to form imines (Gnanaprakasam 2010 and Milstein). Complex 1

is also effective in N—H activation (Khaskin et al.) and in the unique light induced splitting of water to H_2 and O_2 (Kohl et al.).

US patent publication no. US 2009/0112005, to some of the inventors of the present invention, describes methods for preparing amides, by reacting a primary amine and a primary alcohol in the presence of Ruthenium complexes, to generate the amide compound and molecular hydrogen.

PCT patent publication no. WO 2010/018570, to some of the inventors of the present invention, describes methods for preparing primary amines from alcohols and ammonia in the presence of Ruthenium complexes, to generate the amine and water.

Zeng et al., published after the priority date of the present application, describes a process for preparation of polyamides via catalytic dehydrogenation of diols and diamines using PNN pincer ruthenium complexes.

Given the widespread importance of amines, alcohols, amides and esters in biochemical and chemical systems, efficient syntheses that avoid the shortcomings of prior art processes are highly desirable.

SUMMARY OF THE INVENTION

The present invention relates to novel Ruthenium complexes and related borohydride complexes, and the use of such complexes (e.g., catalysts), inter alia, for (1) hydrogenation of amides (including polyamides) to alcohols and amines; (2) preparing amides from alcohols with amines (including the preparation of polyamides (e.g., polypeptides) by reacting dialcohols and diamines and/or by polymerization of amino alcohols); (3) hydrogenation of esters to alcohols (including hydrogenation of cyclic esters (lactones) or cyclic di-esters (di-lactones) or polyesters); (4) hydrogenation of organic carbonates (including polycarbonates) to alcohols and hydrogenation of carbamates (including polycarbamates) or urea derivatives to alcohols and amines; (5) dehydrogenative coupling of alcohols to esters; (6) dehydrogenation of secondary alcohols to ketones; (7) amidation of esters (i.e., synthesis of amides from esters and amines); (8) acylation of alcohols using esters; (9) coupling of alcohols with water to form carboxylic acids; and (10) dehydrogenation of beta-amino alcohols to form pyrazines. The present invention further relates to the novel uses of certain pyridine Ruthenium complexes.

The inventors have unexpectedly discovered new, bipyridine-based pincer complexes of general formulae A1, A2 and A3 as described herein. Examples of such complexes include, but are not limited to, compounds of general formulae B1, C1, B2 and C2, and compounds represented by the structures 3, 4, 7 and 9. Also unexpectedly discovered are borohydride complexes of said bipyridine-based pincer complexes, represented by the structure of general formulae D and E, as well as pyridine-based borohydride complexes of general formulae F, G or H and some borohydride complexes such as 2', 4', 6' and 8'. These compounds efficiently catalyze various processes as described and exemplified herein. In one embodiment, the complex is a pincer complex represented by the structure of formula 3 (FIG. 1B). It has unexpectedly been discovered that complex 3 efficiently catalyzes the unprecedented selective hydrogenation of amides to form amines and alcohols (Scheme 3). The reaction proceeds under mild pressure and neutral conditions, with no additives being required. Since the reaction proceeds well under anhydrous conditions, hydrolysis of the amide is not involved in this process.

Scheme 3

R, R' = H, aryl, alkyl, alkylaryl, et.
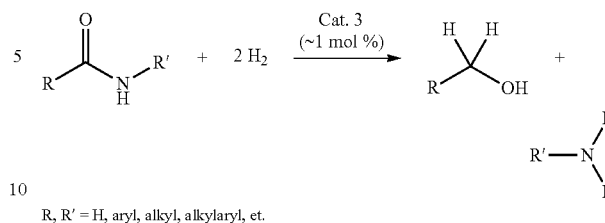
Other reactions catalyzed by pincer complex 3 and the other pincer complexes described herein, and their borohydride derivatives, are described in more detail hereinbelow. The simplicity, generality and excellent atom-economy of these processes make them attractive for use both in small and large scale applications.

In one embodiment, the Ruthenium complex is represented by any one of formulae A1, A2 or A3:

A1

A2

A3

wherein

L^1 is selected from the group consisting of phosphine (PR^{a}R^b), phosphite P(OR^a)(OR^b), phosphinite P(OR^a) (R^b), amine (NR^{a}R^b), imine, oxazoline, sulfide (SR^a), sulfoxide (S(=O)R^a), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^{a}R^b), stibine (SbR^{a}R^b) and a N-heterocyclic carbene represented by the structures:

L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, PR^{a}R^{b}R^c, P(OR^a)(OR^b)(OR^c),

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NO+, AsR^{a}R^{b}R^c, SbR^{a}R^{b}R^c, SR^{a}R^b, nitrile (RCN), isonitrile (RNC), N$_2$, PF$_3$, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;

L^3 is absent or is L^2;

Y and Z are each independently H or an anionic ligand selected from the group consisting of H, halogen, OCOR, OCOCF$_3$, OSO$_2$R, OSO$_2$CF$_3$, CN, OR, N(R)$_2$ and RS;

R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X^1 represents zero one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and anion represents a group bearing a single negative charge; or a borane derivative of said complex.

In one embodiment, X^1 and X^2 are each absent (i.e., the bipyridine moiety is unsubstituted). In another embodiment, L^1 is phosphine (PR^{a}R^b). In another embodiment, L^1 is amine (NR^{a}R^b). In another embodiment, L^2 is CO. Each possibility represents a separate embodiment of the present invention.

In some embodiments, the Ruthenium complex acts as a catalyst (and is thus designated "Ruthenium catalyst").

In one embodiment, the Ruthenium complex is represented by the structure of formula A1. In a particular embodiment of formula A1, the Ruthenium complex is represented by the structure of formula B1. In another particular embodiment of formula A1, the Ruthenium complex is represented by the structure of formula C1. In one embodiment, the Ruthenium complex is represented by the structure of formula 3 (also shown in FIG. 1B).

In another embodiment of the present invention, the Ruthenium complex is represented by the structure of formula A2. In one embodiment of formula A2, the Ruthenium complex is represented by the structure of formula B2. In another particular embodiment of formula A2, the Ruthenium complex is represented by the structure of formula C2.

In one embodiment, Y is halogen, such as chloro. For example, the Ruthenium complex is represented by the structure of formulae 4, 7 or 9.

In another embodiment of the present invention, the Ruthenium complex is represented by the structure of formula A3.

The structures of Ruthenium complexes of Formulae A1, B1, C1, A2, B2, C2, A3, 3, 4, 7 and 9 are described in detail hereinbelow.

In another embodiment, the present invention provides a borane derivative of a Ruthenium complex, the borane derivative represented by the structure of formula F:

F
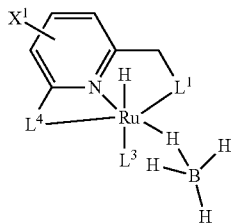
wherein

each L^1 is independently selected from the group consisting of phosphine (PR^{a}R^b), phosphite P(OR^a)(OR^b),

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phosphinite P(OR^a)(R^b), amine (NR^{a}R^b), imine, oxazoline, sulfide (SR^a), sulfoxide (S(=O)R^a), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^{a}R^b), stibine (SbR^{a}R^b) and a N-heterocyclic carbene represented by the structures:
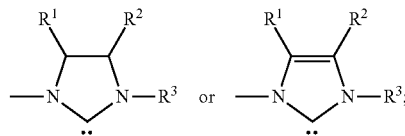
L^3 is absent or is a mono-dentate two-electron donor selected from the group consisting of CO, PR^{a}R^{b}R^c, P(OR^a)(OR^b)(OR^c), NO+, AsR^{a}R^{b}R^c, SbR^{a}R^{b}R^c, SR^{a}R^b, nitrile (RCN), isonitrile (RNC), N$_2$, PF$_3$, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;

L^4 is —CH$_2$-L^1- or a group of the formula:

R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

In some embodiments, the borane derivative is represented by the structure of any of formulae D, E, G and H. It is noted that compounds D and E are borane derivatives of the Ruthenium complex of formula A1 as described hereinabove.

In other embodiments, the borane derivative is represented by the structure of any of formulae 2', 4', 6' and 8'.

The structures of borohydride-Ruthenium complexes of D, E, G, H, 2', 4', 6' and 8' are described in detail hereinbelow.

The present invention further provides various processes which utilize the Ruthenium complexes of the present invention as catalysts.

Thus, in some embodiments, the present invention provides a process for hydrogenating amides (including polyamides and polypeptides) by reacting the amide with molecular hydrogen (H$_2$) in the presence of the Ruthenium complexes of the present invention to generate the corresponding alcohol and amine. As contemplated herein, the inventors have discovered a novel process for converting amides to alcohols and amines in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex, which is represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9, or any other Ruthenium complex covered by such formulae, optionally in the presence of a base. In addition, this reaction is catalyzed by the

Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes of formula A1', A2' and A3' wherein L_1 is $N(R)_2$. The contents of US 2009/0112005 are incorporated by reference herein and the structures of the Ruthenium complexes of formula A1', A2' and A3' are provided hereinbelow. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (FIG. 1A). Each possibility represents a separate embodiment of the present invention.

In a similar manner, lactams (cyclic amides) can be hydrogenated to the corresponding amino alcohols. In addition, polyamides and/or polypeptides can be hydrogenated to the corresponding alcohols and amines.

Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

Similar to the hydrogenation of amides, the novel Ruthenium complexes of the present invention can also catalyze the hydrogenation of esters and organic carbonates to alcohols, or the hydrogenation of carbamates to the corresponding amines and alcohols, or the hydrogenation of urea derivatives to the corresponding amines and methanol. Thus, in other embodiments, the present invention further provides a process for hydrogenating an ester, organic carbonate, carbamate or urea derivative, with molecular hydrogen (H_2) in the presence of the Ruthenium complex, as described herein. As contemplated herein, the inventors have further discovered a novel process for converting esters (e.g., formate esters), organic carbonates, carbamates or urea derivatives to alcohols and/or amines in high yields and high turnover numbers. Polyesters, polycarbonates, polycarbamates and/or polyureas can be hydrogenated in a similar manner. These reactions are catalyzed by a Ruthenium complex, which is represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9 or any other Ruthenium complex covered by such formulae. These reactions are also catalyzed by the borohydride complexes described herein, such as complexes D, E, F, G and H, and compounds 2', 4', 6' and 8'. Currently preferred catalysts (complexes) for hydrogenation of organic carbonates, carbamates and urea derivatives are Ruthenium complexes which are represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9, In some preferred embodiments, hydrogenation of esters is catalyzed by the borohydride complexes described herein, such as complexes D, E, F, G and H, and compounds 2', 4', 6' and 8' Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

In another embodiment, the hydrogenation of organic carbonates, carbamates and urea derivatives to amines and alcohols (including hydrogenation of polycarbonates, polycarbamates and polyurea derivatives) can be catalyzed by any of the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes of formula A1', A2' and A3' wherein L_1 is $N(R)_2$. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (FIG. 1A). Each possibility represents a separate embodiment of the present invention.

In a similar manner, lactones (e.g., cyclic esters) can be hydrogenated to alcohols. For example, cyclic di-esters (di-lactones) can be hydrogenated to the corresponding (vicinal) diols. In one particular embodiment, the present invention is directed to a process comprising hydrogenation of cyclic di-esters (di-lactones), which may be biomass-derived. e.g., glycolide and lactide to the corresponding 1,2-diols (vicinal diols). The process of lactone hydrogenation can be catalyzed by the same complexes described above with respect to hydrogenation of esters to alcohols. In other embodiments, the present invention includes process for hydrogenating

polyesters to the corresponding alcohols. Each possibility represents a separate embodiment of the present invention.

The present invention further provides a process for preparing amides (including polyamides and polypeptides), by reacting an amine and an alcohol in the presence of a Ruthenium complex, to generate the amide compound and molecular hydrogen (H_2). As contemplated herein, the inventors have further discovered a novel process for preparing amides in which primary and secondary amines are directly acylated by equimolar amounts of alcohols to produce amides and molecular hydrogen in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (for complex F preferably L_4 is $CH_2NR^aR^b$), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Use of diamines or dialcohols in the reaction leads to diamides, whereas when diamines and dialcohols are used together, the process results in a polyamide. Similarly, beta-amino alcohols can be dehydrogenated in the presence of the Ruthenium complexes of the present invention to form polypeptides. Also, the process of the invention covers inter or intramolecular coupling of amino alcohols to form lactams, including cyclic peptides (in the case of coupling of beta-amino alcohols).

The amidation or polyamidation reactions (including the coupling of beta-amino alcohols to form polypeptides), can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes in which L_1 is $N(R)_2$. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (FIG. 1A). Other compounds are represented by any of formulae A1', A2' or A3' wherein L_1 is $N(R)_2$ as described herein. Polypeptide (or cyclic peptide) preparation from beta-amino alcohols, catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, namely compounds A1', A2' or A3' wherein L_1 is $N(R)_2$ has not previously been described, and constitutes another embodiment of the present invention.

In some embodiments, beta-amino alcohols can be dehydrogenated in the presence of Ruthenium complexes to form cyclic dipeptides. Such reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (for complex F preferably L_4 is $CH_2NR^aR^b$), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Alternatively, such reactions can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes in which L_1 is $N(R)_2$.

In other embodiments, beta-amino alcohols can be dehydrogenated in the presence of Ruthenium complexes to form pyrazines. Ruthenium complexes which catalyze such reactions are those which contain two phosphnine ligands or N-heterocyclic carbene ligands. Examples of such complexes include borohydride complexes represented by formula F (wherein each one of L^1 and L^4 contain a phosphine and/or N-heterocyclic carbene), G, 2' and 6'. Other Ruthenium complexes which catalyze such reactions are described in US Patent publication US 2009/0112005, in particular Ruthenium complexes of formula A1', A2' and A3' which contain two phosphnine ligands or N-heterocyclic carbene ligands.

The present invention further provides a process for preparing esters by coupling of alcohols in the presence of a

Ruthenium complex, to generate the ester compound and molecular hydrogen. In one embodiment, the process involves coupling of primary alcohols. In another embodiment, the process involves coupling of a primary and secondary alcohol. These reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Use of dialcohols in the reaction leads to polyesters or to lactones.

The present invention further relates to a process for preparing a ketone by dehydrogenation of a secondary alcohol, by reacting the secondary alcohol in the presence of the Ruthenium complex which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae, thereby generating the ester and molecular hydrogen.

The present invention further relates to a process for the coupling of alcohols with water and a base to form carboxylic acid salts, by contacting the alcohol and a base with water in the presence of the Ruthenium complex which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae, thereby generating the carboxylic acid salt and molecular hydrogen. Optionally, the salt can be converted to the carboxylic acid upon reaction with an acid. This reaction can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, such as, but not limited to the compounds of formula A1', A2' and A3', and Pincer complex of Formula 1.

The present invention further provides a process for preparing amides, by reacting an amine and an ester in the presence of a Ruthenium complex, to generate the amide compound and molecular hydrogen (H_2). As contemplated herein, the inventors have further discovered a novel process for preparing amides in which primary and secondary amines are directly reacted with esters to produce amides and molecular hydrogen in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (when complex F is used and L^4 is —CH_2-L^1, L^1 is preferably NR^aR^b), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Reactions of esters with diamines leads to diamides.

The present invention further provides a process for preparing esters by acylation of alcohols using esters in the presence of a Ruthenium complex, to generate the ester compound and molecular hydrogen. In one embodiment, the process involves reaction of primary alcohols and esters. In another embodiment, the process involves reaction of a secondary alcohols and esters. These reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

In some embodiments, the process of any of the embodiments of the present invention as described herein is conducted under neat conditions in the absence of a solvent. In other embodiments, however, the process is conducted in the presence of an organic solvent such as, but not limited to benzene, toluene, o-, m- or p-xylene, mesitylene (1,3,5-trimethyl benzene), dioxane, THF, DME, anisole and cyclohexane.

In some embodiments the process is conducted under heat. In other embodiments, the process is conducted under inert gas. In other embodiments, the process is conducted under heat and under inert gas. However, the reactions of the invention can, when appropriate, also be conducted in the open air.

In one embodiment, the Ruthenium complex of the present invention is represented by the structure of formula A1, and the reactions described herein do not require the presence of a base. In another embodiment, Ruthenium complex is represented by the structure of formula A2. When Z is H and Y is other than H, the process further comprises adding at least one equivalent of a base relative to the Ruthenium complex. When Z and Y are other than H, the process further comprises adding at least two equivalents of a base relative to the Ruthenium complex. When Z and Y are both H, the process is conducted in the absence of a base. In another embodiment, Ruthenium complex is represented by the structure of formula A3. When Z is H, the process further comprises adding at least one equivalent of a base relative to the Ruthenium complex. When Z is other than H, the process further comprises adding at least two equivalents of a base relative to the Ruthenium complex.

Also encompassed by the present invention are certain intermediate compounds and their use in the preparation of the Ruthenium complexes of the present invention. Thus, in one embodiment, the present invention relates to a compound represented by the structure of formula Z:
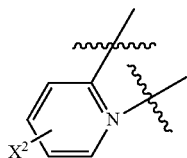

wherein

L^1 is selected from the group consisting of phosphine (PR^{a}R^b), phosphite P(OR^a)(OR^b), phosphinite P(OR^a) (R^b), amine (NR^{a}R^b), imine, oxazoline, sulfide (SR^a), sulfoxide (S(=O)R^a), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^{a}R^b), stibine (SbR^{a}R^b) and a N-heterocyclic carbene represented by the structures:

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected

from the group consisting of alkyl, cycloalkyl, aryl, het-
erocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkyl-
heterocyclyl, alkylheteroaryl, halogen, nitro, amide,
ester, cyano, alkoxy, alkylamino, arylamino, an inor-
ganic support and a polymeric moiety; and

R^a and R^b are each independently alkyl, cycloalkyl, aryl,
heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl,
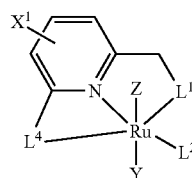alkylheterocyclyl or alkylheteroaryl.

In some embodiments, the compound selected from the
group consisting of

and
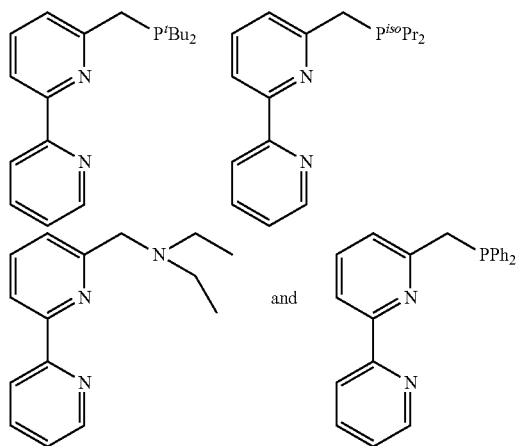
BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be understood and appreciated
more fully from the following detailed description taken in
conjunction with the appended figures:

FIG. **1**: shows the structure of dearomatized PNN pincer
complexes 1 and 2 (FIG. **1A**) and complex 3 (FIG. **1B**).

FIG. **2**: shows the X-ray structure of Ruthenium complex 4
with the thermal ellipsoids at 50% probability level. All C—H
hydrogen atoms are omitted for clarity.

FIG. **3**: shows the X-ray structure of Ruthenium borohy-
ride complex 2' with the thermal ellipsoids at 50% probability
level. All C—H hydrogen atoms are omitted for clarity.

FIG. **4**: shows the variable-temperature (213K-373K) ^{1}H
NMR of Ruthenium borohydride complex 4' in the region of
Ru—H and BH_4^- ligands (toluene-d_8 as solvent).

FIG. **5**: shows MALDI-TOF mass spectra of polyamides
synthesized by the processes of the present invention. FIG.
5A: polyamide 3a in TFA using HBA matrix. FIG. **5B**: polya-
mide 3c in TFA using HBA matrix. FIG. **5C**: polyamide 3d in
50% TFA/DCM using HBA-NaI. FIG. **5D**: polyamide 3e in
TFA using HBA matrix. FIG. **5E**: polyamide 3h in TFA using
HBA matrix.

FIG. **6**: TGA of polyamides 3.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

The present invention provides novel Ruthenium based
complexes and catalysts and borohydride complexes thereof,
and the use of such complexes for, inter alia, (1) hydrogena-
tion of amides (including polyamides) to alcohols and
amines; (2) preparing amides from alcohols with amines (in-
cluding the preparation of polyamides (e.g., polypeptides) by
reacting dialcohols and diamines and/or by polymerization of
amino alcohols); (3) hydrogenation of esters to alcohols (in-

cluding hydrogenation of cyclic esters (lactones) or cyclic
di-esters (lactones) or polyesters); (4) hydrogenation of
organic carbonates (including polycarbonates) to alcohols
and hydrogenation of carbamates (including polycarbam-
ates) or urea derivatives to alcohols and amines; (5) dehydro-
genative coupling of alcohols to esters; (6) dehydrogenation
of secondary alcohols to ketones; (7) amidation of esters (i.e.,
synthesis of amides from esters and amines); (8) acylation of
alcohols using esters; (9) coupling of alcohols with water to
form carboxylic acids; and (10) dehydrogenation of beta-
amino alcohols to form pyrazines. The present invention fur-
ther relates to the novel uses of certain pyridine Ruthenium
complexes.

Ruthenium Complexes

In one embodiment, the Ruthenium complex is represented
by any one of formulae A1, A2 or A3:

wherein

L^1 is selected from the group consisting of phosphine
(PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)$
(R^b), amine (NR^aR^b), imine, oxazoline, sulfide (SR^a),
sulfoxide ($S(\equiv O)R^a$), heteroaryl containing at least one
heteroatom selected from nitrogen and sulfur; arsine
(AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic car-
bene represented by the structures:

L^2 is a mono-dentate two-electron donor selected from the
group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$,
NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN),
isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahy-
drothiophene, alkene and alkyne;

L^3 is absent or is L^2;

Y and Z are each independently H or an anionic ligand selected from the group consisting of H, halogen, OCOR, OCOCF$_3$, OSO$_2$R, OSO$_2$CF$_3$, CN, OR, N(R)$_2$ and RS;

R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and anion represents a group bearing a single negative charge; or a borane derivative of said complex.

In one embodiment, X^1 and X^2 are absent (i.e, the bipyridine moiety is unsubstituted). In another embodiment, L^1 is phosphine (PR^{a}R^b). In another embodiment, L^2 is CO.

In one embodiment, the Ruthenium complex is represented by the structure of formula A1:
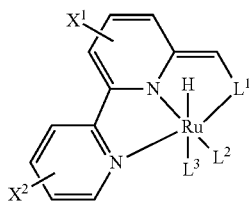
A1

In a particular embodiment of formula A1, the Ruthenium complex is represented by the structure of formula B1. In another particular embodiment of formula A1, the Ruthenium complex is represented by the structure of formula C1.

B1

C1
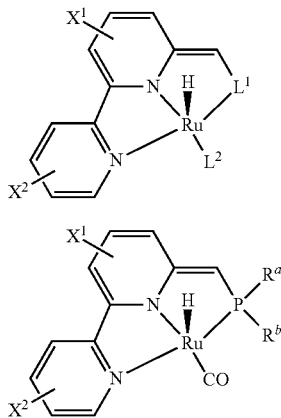
Each of L^1, L^2, X^2, R^a and R^b in Formulae B1 and C1 are as defined for formula A1. Each possibility represents a separate embodiment of the present invention.

In one embodiment, each of R^a and R^b is tert-butyl. In another currently, each of R^c and R^d are isopropyl. Each possibility represents a separate embodiment of the present invention.

In one embodiment, the Ruthenium complex is represented by the structure of formula 3 (also shown in FIG. 1B).

3

In another embodiment of the present invention, the Ruthenium complex is represented by the structure of formula A2:

A2
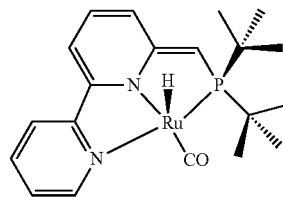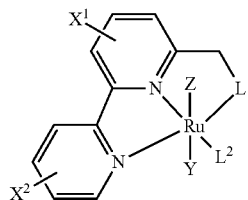
In one embodiment of Formula A2, Z and Y are either each H, each a halogen (e.g., F, Cl, Br, I) or one of Z and Y is H and the other a halogen. Each possibility represents a separate embodiment of the present invention.

In one particular embodiment, Z is H and Y is other than H in formula A2. When such a complex is used, the processes of the invention as described hereinbelow are typically conducted in the presence of at least one equivalent of a base relative to the Ruthenium complex. In another particular embodiment, each of Z and Y is other than H in formula A2. When such a complex is used, the processes of the invention as described hereinbelow are typically conducted in the presence of at least two equivalents of a base relative to the Ruthenium complex. In another particular embodiment, Z and Y are both H in formula A2. When such a complex is used, no base is required for the processes of the invention.

In one embodiment of formula A2, the Ruthenium complex is represented by the structure of formula B2:

B2
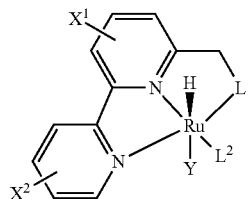
In another particular embodiment of formula A2, the Ruthenium complex is represented by the following structure of formula C2:

C2
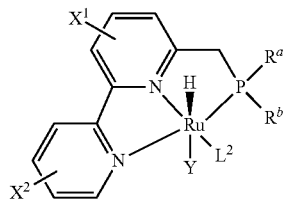
Each of L^1, L^2, X^1, X^2, Y, R^a and R^b in formulae B2 and C2 are as defined in formula A2. Each possibility represents a separate embodiment of the present invention.

In one embodiment, Y is halogen, such as chloro. For example, the Ruthenium complex may be represented by the structure of any of formulae 4, 7 or 9:
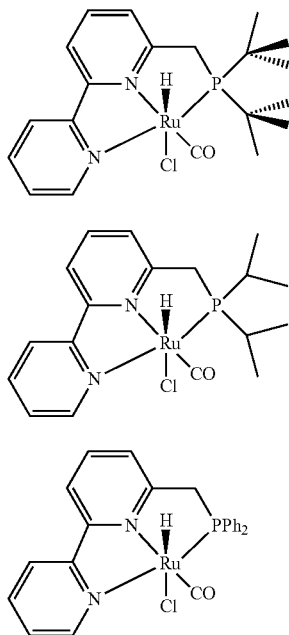
In another embodiment of the present invention, the Ruthenium complex is represented by the structure of formula A3:

A3
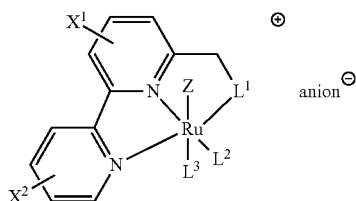
In one particular embodiment, Z is H in formula A3. When such a complex is used, the processes of the invention as described hereinbelow are typically conducted in the presence of at least one equivalent of a base relative to the Ruthenium complex. In another particular embodiment, Z is other than H in formula A3. When such a complex is used, the processes of the invention as described hereinbelow are typically conducted in the presence of at least two equivalents of a base relative to the Ruthenium complex.

Compounds of formula A2 and formula A3 are precursors of compounds of formula A1. Additionally some precursors of the complexes of formula A1 include, but are not limited to, compounds of general formulae (i), (ii) and (iii):

(i)

-continued

(ii)

(iii)
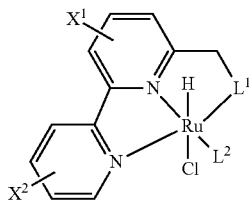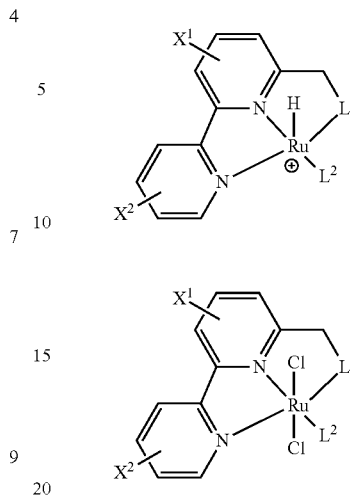
It is understood that any one or more of the precursors can themselves function as complexes in the process of the present invention. For example, when structures (i) and (ii) and their equivalents are used, at least one equivalent of base relative to the Ruthenium complex can be used (e.g., alkoxide, hydroxide). Alternatively, when structure (iii) or its equivalents are used, at least two equivalents of base relative to the Ruthenium complex can be used. Non-limiting examples of bases are alkoxide (e.g., t-butoxide, methoxide, ethoxide), or hydroxide.

Borohydride Complexes:

It has been unexpectedly discovered that certain reactions such conversion of primary alcohols to esters, as well as the dehydrogenation of secondary alcohols to ketones, as well as other reactions contemplated herein, can be effectively accomplished with stable, readily synthesized PNN- and PNP Ru borohydride complexes, in the absence of a base, under mild and neutral conditions, optionally in the absence of hydrogen acceptor.

Thus, in one embodiment, the present invention provides a borane derivative of a Ruthenium complex, the borane derivative represented by the structure of formula F:

F

wherein

each L^1 is independently selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$ phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:

L³ is absent or is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$, NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl and tetrahydrothiophene;

L⁴ is —CH_2-L¹- or a group of the formula:

R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R¹, R² and R³ are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X¹ represents zero, one, two or three substituents and X² represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

In some embodiments, the borane derivative is represented by the structure of any of formulae D, E, G and H. Each possibility represents a separate embodiment of the present invention. It is noted that compounds D and E are borane derivatives of the Ruthenium complex of formula A1 as described hereinabove.

G

H

-continued

D

E
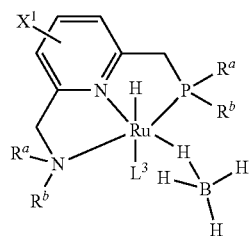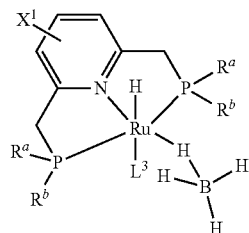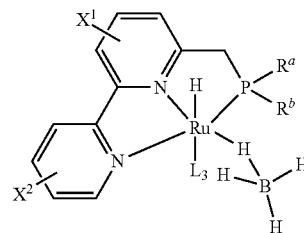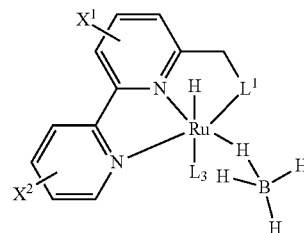
In some other embodiments, the borane derivative is represented by the structure of any of formulae 2', 4', 6' and 8'. Each possibility represents a separate embodiment of the present invention.

2'

4'

6'

-continued

8'
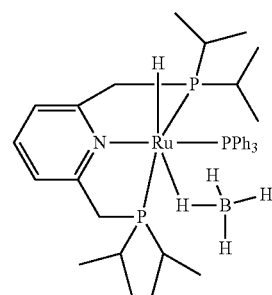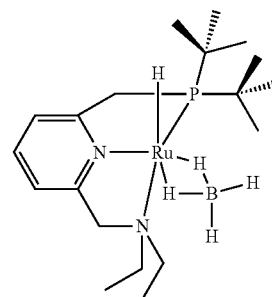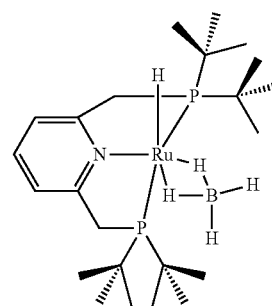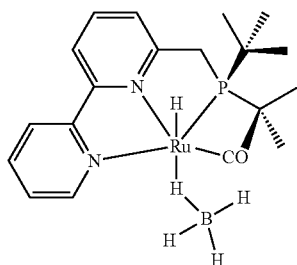
The present invention further provides processes for preparing the novel boronated derivatives of Ruthenium based catalytic complexes. Thus, in one embodiment, the present invention provides a process for preparing a Ruthenium complex represented by the structure of formula D

D

by reacting sodium borohydride ($NaBH_4$) with a precursor of formula A2

A2

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)$ (R^b), amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:

L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^b)$ NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;

L^3 is absent or is L^2;

Y and Z are each independently halogen, $OCOCF_3$, OSO_2R or OSO_2CF_3,

R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

In another embodiment, the present invention provides a process for preparing a borane derivative of a Ruthenium complex represented by the structure of formula F
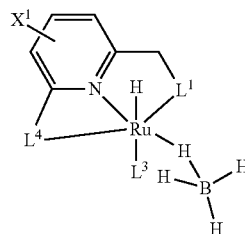
F

the process comprising the step of reacting sodium borohydride ($NaBH_4$) with a precursor of formula

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)$ (R^b), amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:
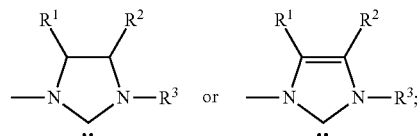
L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$, NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;

L^3 is absent or is L^2;

L^4 is —CH_2-L^1- or a group of the formula:
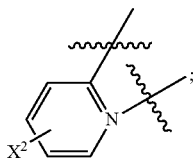
Y and Z are each independently halogen, $OCOCF_3$, OSO_2R or OSO_2CF_3, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

Chemical Definitions

As used herein, the term alkyl, used alone or as part of another group, refers, in one embodiment, to a "C_1 to C_{12} alkyl" and denotes linear and branched, saturated or unsaturated (e.g., alkenyl, alkynyl) groups, the latter only when the number of carbon atoms in the alkyl chain is greater than or equal to two, and can contain mixed structures. Non-limiting examples are alkyl groups containing from 1 to 6 carbon atoms (C_1 to C_6 alkyls), or alkyl groups containing from 1 to 4 carbon atoms (C_1 to C_4 alkyls). Examples of saturated alkyl groups include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, amyl, tert-amyl, hexyl, Examples of alkenyl groups include, but are not limited to, vinyl, allyl, butenyl and the like. Examples of alkynyl groups include, but are not limited to, ethynyl, propynyl and the like. Similarly, the term "C_1 to C_{12} alkylene" denotes a bivalent radical of 1 to 12 carbons.

The alkyl group can be unsubstituted, or substituted with one or more substituents selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylaryl amino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups. Any substituents can be unsubstituted or further substituted with any one of these aforementioned substituents. By way of illustration, an "alkoxyalkyl" is an alkyl that is substituted with an alkoxy group.

The term "cycloalkyl" used herein alone or as part of another group, refers to a "C_3 to C_8 cycloalkyl" and denotes any unsaturated or unsaturated (e.g., cycloalkenyl, cycloalkynyl) monocyclic or polycyclic group. Nonlimiting examples of cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl. Examples or cycloalkenyl groups include cyclopentenyl, cyclohexenyl and the like. The cycloalkyl group can be unsubstituted or substituted with any one or more of the substituents defined above for alkyl. Similarly, the term "cycloalkylene" means a bivalent cycloalkyl,

as defined above, where the cycloalkyl radical is bonded at two positions connecting together two separate additional groups.

The term "aryl" used herein alone or as part of another group denotes an aromatic ring system containing from 6-14 ring carbon atoms. The aryl ring can be a monocyclic, bicyclic, tricyclic and the like. Non-limiting examples of aryl groups are phenyl, naphthyl including 1-naphthyl and 2-naphthyl, and the like. The aryl group can be unsubstituted or substituted through available carbon atoms with one or more groups defined hereinabove for alkyl. An alkylaryl group denotes an alkyl group bonded to an aryl group (e.g., benzyl).

The term "heteroaryl" used herein alone or as part of another group denotes a heteroaromatic system containing at least one heteroatom ring atom selected from nitrogen, sulfur and oxygen. The heteroaryl contains 5 or more ring atoms. The heteroaryl group can be monocyclic, bicyclic, tricyclic and the like. Also included in this expression are the benzoheterocyclic rings. If nitrogen is a ring atom, the present invention also contemplates the N-oxides of the nitrogen containing heteroaryls. Nonlimiting examples of heteroaryls include thienyl, benzothienyl, 1-naphthothienyl, thianthrenyl, furyl, benzofuryl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, isoindolyl, indazolyl, purinyl, isoquinolyl, quinolyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, carbolinyl, thiazolyl, oxazolyl, isothiazolyl, isoxazolyl and the like. The heteroaryl group can be unsubstituted or substituted through available atoms with one or more groups defined hereinabove for alkyl.

The term "heterocyclic ring" or "heterocyclyl" used herein alone or as part of another group denotes a five-membered to eight-membered rings that have 1 to 4 heteroatoms, such as oxygen, sulfur and/or nitrogen. These five-membered to eight-membered rings can be saturated, fully unsaturated or partially unsaturated. Non-limiting examples of heterocyclic rings include piperidinyl, piperidinyl, pyrrolidinyl pyrrolinyl, pyrazolinyl, pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl, indolinyl, dihydrofuranyl, tetrahydrofuranyl, dihydrothiophenyl, tetrahydrothiophenyl, dihydropyranyl, tetrahydropyranyl, and the like. The heterocyclyl group can be unsubstituted or substituted through available atoms with one or more groups defined hereinabove for alkyl.

The inorganic support which is attached to the bipyridine ring can be, for example, silica, silica gel, glass, glass fibers, titania, zirconia, alumina and nickel oxide.

The polymer which is attached to the bipyridine pyridine ring can be, for example, selected from polyolefins, polyamides, polyethylene terephthalate, polyvinylchloride, polyvinylidenechloride, polystyrene, polymethracrylate, natural rubber, polyisoprene, butadiene-styrene random copolymers, butadiene acrylonitrile copolymers, polycarbonate, polyacetal, polyphenylenesulfide, cyclo-olefin copolymers, styrene-acrylonitrile copolymers, ABS, styrene-maleic anhydride copolymers, chloroprene polymers, isobutylene copolymers, polystyrene, polyethylene, polypropylene, and the like.

The term "anion" as used herein refers to any moiety or group bearing a negative charge. Examples of anionic moieties include, but are not limited to halogen (e.g., F, Cl, Br, I), OCOR', OCOCF$_3$, OSO_2R', OSO_2CF_3, BF_4, PF_6, SbF_6, BR_4, ClO_4, $AlCl_4$, CN, OH, OR' or NR'_2 wherein R' is selected from alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein each of the alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl is as defined above.

Novel Processes

The present invention further provides various processes which utilize the Ruthenium complexes of the present invention as catalysts.

In general, the processes of the present invention can be conducted in the absence or in the presence of a solvent. When a solvent is present, it can be an organic solvent, including but not limited to benzene, toluene, o-, m- or p-xylene mesitylene (1,3,5-trimethyl benzene), dioxane, THF, DME, anisole and cyclohexane.

The stoichiometric ratios of reagents can vary, and depend on the particular alcohol, amine, amide, ester etc., being used, as well as solvent used for the reaction. The reactions of the present invention can be performed for as long as needed so as to effect desired transformation, for example 1 hr to 24 hr or longer than 24 hr. The temperature range can vary from room temperature to heated conditions, for example up to 200° C.

1. Hydrogenation of Amides to Alcohols and Amines

The present invention provides a process for hydrogenating amides (including polyamides and polypeptides) by reacting the amide with molecular hydrogen (H_2) in the presence of the Ruthenium complexes of the present invention to generate the corresponding alcohol and amine. As contemplated herein, the inventors have discovered a novel process for converting amides to alcohols and amines in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex, which is represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9 or any other Ruthenium complex covered by such formulae. In addition, this reaction is catalyzed by any of the Ruthenium complexes described in US Patent publication US 2009/0112005, the contents of which are incorporated by reference herein. The compounds of US 2009/0112005 are pyridine based derivatives represented by the structure of formula A1', A2' and A3'. Compounds which catalyze hydrogenation of amides to alcohols and amines are those wherein L_1 is $N(R)_2$:

A1'

A2'

A3'
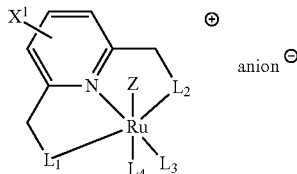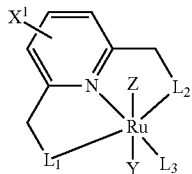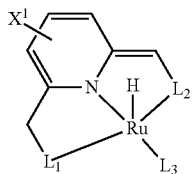
wherein
L_1 is $N(R)_2$,
L_2 is selected from the group consisting of nucleophilic carbene (:$C(R)_2$), $P(R)_2$, $P(OR)_2$, $N(R)_2$, imine, SR, SH, $S(=O)R$, heteroaryl wherein the heteroatom is selected

from nitrogen and sulfur, $As(R)_2$, $Sb(R)_2$ and an N-heterocyclic carbene represented by the structure:

each of R, R^2 and R^3 are independently selected from the group consisting of alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
L_3 is a mono-dentate two-electron donor selected from the group consisting of CO, $P(R)_3$, $P(OR)_3$, NO^+, $As(R)_3$, $Sb(R)_3$, $S(R)_2$, nitrile (RCN) and isonitrile (RNC) wherein R is as defined above;
L_4 is absent or is L_3;
Y and Z are each independently H or an anionic ligand selected from the group consisting of halogen, OCOR, $OCOCF_3$, OSO_2R, OSO_2CF_3, CN, OH, OR, $N(R)_2$, RS and SH; wherein R is as defined above;
X represents zero, one, two or three substituents selected from the group consisting of alkyl, aryl, halogen, nitro, amide, ester, cyano, alkoxy, cycloalkyl, alkylaryl, heterocyclyl, heteroaryl, an inorganic support and a polymeric moiety; and
anion represents a group bearing a single negative charge.

One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (FIG. 1A).

Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

The process of the invention, i.e., the direct catalytic conversion of amides to alcohols and amides is illustrated in Scheme 4. This novel, environmentally benign reaction can be used to prepare alcohols and amines from any type of amide, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste. Thus, in one embodiment, the present invention provides a process for hydrogenating an amide represented by the formula $R^4C(=O)\!-\!N\!-\!R^5R^{5'}$ to an alcohol of formula R^4CH_2OH and amine of formula $R^5R^{5'}NH$:

Scheme 4
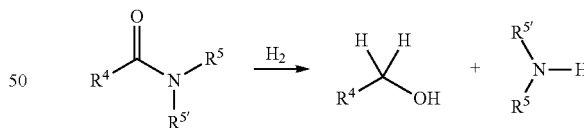
wherein R^4, R^5 and $R^{5'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

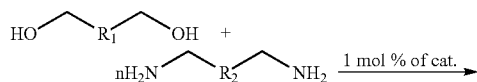A variety of amides can be used in the process of the invention. In some embodiments, the amide is selected from the group consisting of N-benzyl-2-methoxyacetamide, N-hexyl-2-methoxyacetamide, N-hexyl-3-methyloxetane-3-carboxamide, N-hexyl-2-furanylcarboxamide, N-benzylbenzamide, N-ethylacetamide, N-methylpropionamide, N-cyclohexyl-2-methoxyacetamide, N-phenylacetamide, N-phenylhexylamide, 2-methoxy-N-phenylacetamide, N-phenylbenzamide, Ethylenediamine-N,N'-(2-methoxyacetamide), N-hexanoylmorpholine, N-butanoylmorpholine,

N-2-metoxyacetylpyrrolidine, N-formylmorpholine, N,N-dimethylformamide, N,N-diethylbenzamide, benzamide, 4-methylbenzamide, cyclohexanecarboxamide, hexanamide, acetamide, acrylamide and pivalamide. Each possibility represents a separate embodiment of the present invention.

In a similar manner, cyclic amides (lactams) can be hydrogenated to the corresponding amino alcohols. In one embodiment, the lactam is a cyclic peptide, which can be hydrogenated with the Ruthenium complex of the present invention to the respective amino alcohol. In a similar manner, polyamides can be hydrogenated to amines and alcohols, and polypeptides can be hydrogenated to amino alcohols.

2. Hydrogenation of Esters, Organic Carbonates, Carbamates and Urea Derivatives

Similar to the hydrogenation of amides, the novel Ruthenium complexes of the present invention can also catalyze the hydrogenation of esters, hydrogenation of organic carbonates, hydrogenation of carbamates, or hydrogenation of urea derivatives to the corresponding amines and/or alcohols. Thus, in some embodiments, the present invention further provides a process for hydrogenating an ester, organic carbonate, carbamate or urea derivative with molecular hydrogen (H_2) in the presence of the Ruthenium complex of the present invention. As contemplated herein, the inventors have discovered a novel process for converting esters (e.g., formate esters), organic carbonates, carbamates and/or urea derivatives to alcohols and/or amines in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex, which is represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9 or any other Ruthenium complex covered by such formulae. These reactions are also catalyzed by the borohydride complexes described herein, such as complexes D, E, F, G and H, and compounds 2', 4', 6' and 8'. Currently preferred complexes for hydrogenation of organic carbonates, carbamates and urea derivatives are Ruthenium complexes which are represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9. In some preferred embodiments, hydrogenation of esters is catalyzed by the borohydride complexes described herein, such as complexes D, E, F, G and H, and compounds 2', 4', 6' and 8'. Again, depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

In other embodiments, the hydrogenation of organic carbonates, carbamates and urea derivatives can be catalyzed by any of the Ruthenium complexes described in US Patent publication US 2009/0112005, the contents of which are incorporated by reference herein. Examples of such compounds are compounds of formula A1', A2' and A3' wherein L_1 is $N(R)_2$, as described above with respect to processes for hydrogenation of amides to amines and alcohols.

One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (FIG. 1A).

One embodiment of the process of the invention, i.e., the direct catalytic conversion of esters to alcohols, is illustrated in Scheme 5A, whereby an ester represented by the formula $R^6C(=O)$—OR^7 is hydrogenated to the corresponding alcohol or alcohols:
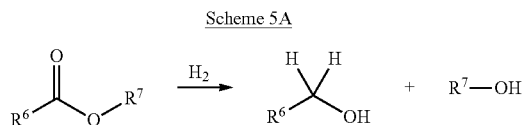
Scheme 5A

wherein R^6 is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and R^7 is selected

from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

It is apparent to a person of skill in the art that when the ester is symmetric (i.e., $R^6=R^7$), the reaction yields two equivalents of the same alcohol. However, when the ester is asymmetric (i.e., R^6 is different from R^7), the reaction yields a mixture of two alcohols.

In one embodiment, R^6 is H and the process comprises hydrogenating a formate ester of formula H—C(=O)—OR^7 to methanol and an alcohol of formula R^7—OH.

A variety of esters can be used in the process of the invention. In some embodiments, the ester is selected from the group consisting of hexyl hexanoate, butyl butyrate, methyl formate, ethyl formate, propyl formate and butyl formate. In other embodiments, the ester is a cyclic ester (a lactone). In yet other embodiments, the ester is a cyclic di-ester (di-lactone).

In yet other embodiments, the ester is a biomass-derived cyclic di-ester (di-lactone) such as, but not limited to glycolide or lactide. In yet another embodiment, the ester is polyester. Each possibility represents a separate embodiment of the present invention.

Catalytic homogeneous hydrogenation of cyclic di-esters (di-lactone), specifically glycolide and lactide to the corresponding 1,2-diols (vicinal diols) is of significant interest conceptually and practically, since these compounds are produced from biomass sources such as glycolic acid and lactic acid respectively via self-esterification, and their efficient hydrogenation can provide an alternative, mild approach to the indirect transformation of biomass resources to important synthetic building blocks. As contemplated herein, the unprecedented, environmentally benign, atom-economical route for the synthesis of propylene glycol and ethylene glycol are efficiently catalyzed by bipyridine based PNN—Ru (II) dearomatized pincer complex of formula (1), as well as other Ruthenium complexes as described herein. These catalytic reactions proceed under neutral, homogeneous conditions, at mild temperatures and mild hydrogen pressures. The optical purity of a chiral diol is unaffected during the hydrogenation reactions.

The process of lactone or di-lactone hydrogenation can be catalyzed by the same complexes described above with respect to hydrogenation of esters to alcohols.

Scheme 5B
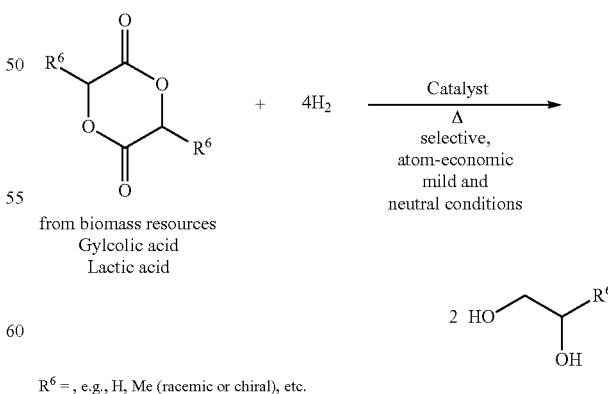
wherein R^6 is as described above.

A variety of cyclic di-esters (di-lactones) can be used in the process of the invention. In some embodiments, the ester is a

biomass-derived cyclic di-ester (di-lactone) such as, but not limited to glycolide or lactide. Each possibility represents a separate embodiment of the present invention.

Another embodiment of the process of the invention, i.e., the direct catalytic hydrogenation of organic carbonates, is illustrated in Scheme 6, whereby a carbonate represented by the formula R^8O—$C(=O)$—$OR^{8'}$ is hydrogenated to the corresponding alcohols(s) and methanol:

Scheme 6

$$R^8 \diagdown O \diagup \overset{\overset{O}{\|}}{C} \diagdown O \diagup R^{8'} \xrightarrow{H_2} R^8\text{—OH} + R^{8'}\text{—OH} + CH_3OH$$
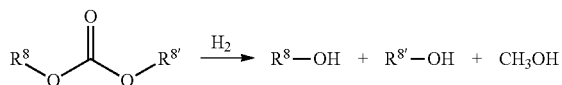
wherein R^8 and $R^{8'}$ are the same or different and are selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

It is apparent to a person of skill in the art that when the organic carbonate is symmetric (i.e., $R^8=R^{8'}$) the reaction yields two equivalents of the same alcohol, and one equivalent of methanol. However, when the organic carbonate is asymmetric (i.e., R^8 is different from $R^{8'}$), the reaction yields a mixture of two alcohols, and methanol.

A variety of organic carbonates can be used in the process of the invention. In some embodiments, the carbonate is dimethyl carbonate, diethyl carbonate, dipropyl carbonate or dibutyl carbonate. In another embodiment, the carbonate is a polycarbonate, such as polyethylene carbonate or polypropylene carbonate. Each possibility represents a separate embodiment of the present invention.

Another embodiment of the process of the present invention, i.e., the direct catalytic hydrogenation of carbamates, is illustrated in Scheme 7A, whereby a carbamate represented by the formula R^{90}—$C(=O)$—NHR^{10} is hydrogenated to the corresponding amine, alcohol and methanol:

Scheme 7A

$$R^9O \diagdown \overset{\overset{O}{\|}}{C} \diagdown \underset{H}{N} \diagup R^{10} \xrightarrow{H_2} R^9\text{—OH} + R^{10}\text{—}\underset{H}{\overset{H}{N}} + CH_3OH$$
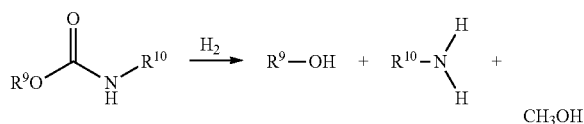
wherein R^9 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and R^{10} is selected from the group consisting of H or an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

A variety of organic carbamates can be used in the process of the invention. In some embodiments, the carbamate is methyl benzylcarbamate or methyl 4-methoxybenzylcarbamate. In another embodiment, the carbamate is a polycarbamate. Each possibility represents a separate embodiment of the present invention.

Another embodiment of the process of the present invention, i.e., the direct catalytic hydrogenation of urea derivatives, is illustrated in Scheme 7B, whereby a urea derivative is hydrogenated to the corresponding amine(s) and methanol:

Scheme 7B

$$R^{9a} \diagdown \underset{R^{9b}}{N} \diagup \overset{\overset{O}{\|}}{C} \diagdown \underset{R^{10b}}{N} \diagup R^{10a} + 3 H_2 \xrightarrow[\Delta]{Catalyst} MeOH +$$

$$R^{9a}\text{—}\underset{R^{9b}}{\overset{\overset{H}{N}}{}} + R^{10a}\text{—}\underset{R^{10b}}{\overset{\overset{H}{N}}{}}$$
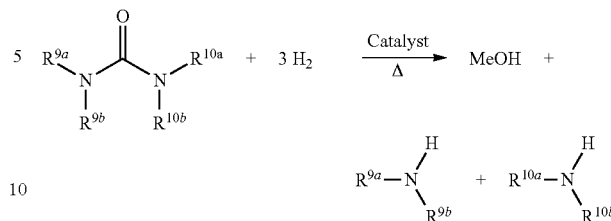
wherein each of R^{9a} and R^{10a}, which may be the same or different, is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, and heterocyclyl, and each of R^{9b} and R^{10b}, which may be the same or different, is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, and heterocyclyl. Alternatively, at least one of R^{9a} and R^{10a}, and/or R^{9b} and R^{10b} together with the nitrogen to which they are attached form a heterocyclic ring.

A variety of symmetrical ($R^{9a}=R^{10a}$, $R^{9b}=R^{10b}$) and asymmetrical ($R^{9a}{\neq}R10^a$, $R^{9b}{\neq}R^{10b}$) urea derivatives can be used in the process of the invention, with each possibility representing a separate embodiment of the present invention. In some embodiments, the urea derivative is 1,3-dimethylurea, and the product of the reaction is methanol and two molecules of methylamine. In another embodiment, the urea derivative is selected from the group consisting of 1,3-dipropylurea, 1,3-dihexylurea, 1,3-bis(2-methoxyethyl)urea, 1,3-dicyclohexylurea, 1,3-dibenzylurea, 1,3-bis(4-methylbenzyl)urea, 1,3-bis(4-methylbenzyl)urea, 1,3-diphenylurea, 1,3-bis(4-(tert-butyl)phenyl)urea, 1,1,3,3-tetramethylurea, and di(piperidin-1-yl)methanone. Polyurea derivatives can also be hydrogenated in a similar manner. Each possibility represents a separate embodiment of the present invention.

3. Dehydrogenative Coupling of Alcohols and Amines with Liberation of H_2 to Form Amides or of Beta-Amino Alcohols to Form Pyrazines:

The present invention further provides a process for preparing amides, by reacting an amine and an alcohol in the presence of a Ruthenium complex, to generate the amide compound and molecular hydrogen (H_2). As contemplated herein, the inventors have further discovered a novel process for preparing amides in which primary and secondary amines are directly acylated by equimolar amounts of alcohols to produce amides and molecular hydrogen in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (when complex F is used and L^4 is —CH_2-L^1, L^1 is preferably NR^aR^b), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

Use of diamines or dialcohols in the reaction leads to diamides, whereas when diamines and dialcohols are used together, the process results in a polyamide. Furthermore, reactions of amino-alcohols results in cyclic amides (lactams). For example, reaction of $H_2N(CR^1R^2)_nCH_2OH$ results in lactams for n=4, 5 or 6, such as caprolactam for n=6 and $R^1=R^2=H$. For n>6, the reaction typically results in polymers. In another embodiment, when amino alcohols such as R—$CH(NH_2)CH_2OH$ are used, peptides or polypeptides are

formed (e.g., dehydrogenation of alaninol with the Ruthenium complexes of the present invention results in polyalanine).

The process of the invention, i.e., the direct catalytic conversion of alcohols and amines into amides and dihydrogen is illustrated in Scheme 8A. In accordance with this process, an amine represented by formula $R^{11}R^{11'}NH$ is reacted with an alcohol represented by the formula $R^{12}CH_2OH$ to generate an amide represented by the structure R^{12}—C(=O)—$NR^{11}R^{11'}$. This novel, environmentally benign reaction can be used to produce various amides from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.

Scheme 8A
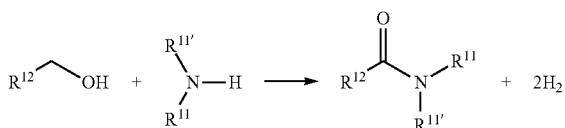
$$R^{12} \diagup OH \ + \ \underset{R^{11}}{\overset{R^{11'}}{N}}-H \ \longrightarrow \ R^{12}\overset{O}{\underset{R^{11'}}{C}}\underset{R^{11'}}{N}R^{11} \ + \ 2H_2$$

wherein R^{10}, R^{11} and R^{12} are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein R^{10}, R^{11} and R^{12} can be the same or different from each other.

A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, and 2-methyl-1-butanol. Each possibility represents a separate embodiment of the present invention.

A variety of primary and secondary amines (as well as ammonia) may be used in the process of the invention. In some embodiments, the amine is selected from the group consisting of benzylamine, 1-hexylamine, 1-pentylamine, 1-(2-furyl)methylamine, aniline, morpholine, pyrrolidine, 2-methylhexylamine, and cyclohexylamine. Each possibility represents a separate embodiment of the present invention.

In another embodiment, the process of the invention can also be applied to bis-acylation reactions with diamines. Upon reacting alcohols and diamines, the corresponding bis-amides are produced in high yields. In some embodiments, the diamine is ethylenediamine, diethylenetriamine or 1,6-diaminohexane.

Similarly, when diamines and dialcohols are used, polyamides or peptides are obtained. The applicants have surprisingly discovered that Ruthenium complexes catalyze the synthesis of polyamides directly from diols and diamines. This polyamidation reaction is general, environmentally benign and atom economical. It proceeds under neutral reaction conditions without the use of activators, condensing agents or other additives. A preferable solvent for use in this reaction is 1,4-dioxane, however other solvents can be used as apparent to a person of skill in the art. Moreover, these methods produce H_2 as the only byproduct (Scheme 8B):

Scheme 8B

$$HO \diagup R_1 \diagdown OH \ + \ nH_2N \diagup R_2 \diagdown NH_2 \ \xrightarrow{\text{1 mol \% of cat.}}$$

-continued

$$\left[\begin{array}{c} \overset{O}{\underset{X}{\parallel}} \diagup R_1 \overset{O}{\underset{\underset{H}{N}}{\parallel}} \diagup R_2 \underset{\underset{H}{N}}{\diagup} \end{array}\right]_n Y \ + \ 4nH_2$$
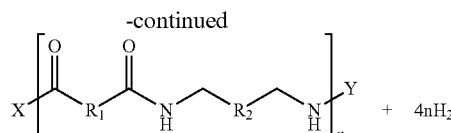
A variety of dialcohols can be used for this reaction, non-limiting examples of which include hexane-1,2-diol, octane-1,8-diol, 1,3-phenylenedimethanol, (5-methoxy-1,3-phenylene)dimethanol, 1,4-phenylenedimethanol, pyridine-2,6-diyldimethanol, pentane-1,5-diol, cyclohexane-1,4-diyldimethanol, and (5-(hexyloxy)-1,3-phenylene) dimethanol.

A variety of diamines can be used for this reaction, non-limiting examples of which include hexane-1,6-diamine, ethane-1,2-diamine, 1,3-phenylenedimethanamine, and 1,4-phenylenedimethanamine. The reaction between the amine and alcohol can be inter-molecular (i.e., the amine and the alcohol are present in separate molecules). Alternatively, the reaction between the amine and alcohol can be intra-molecular, i.e., the amine and alcohol functionalities can be present in the same molecule, resulting in intra-molecular cyclization to generate a lactam.

In addition, the aforementioned amidation and polyamidation reactions are also catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes in which L_1 is $N(R)_2$, as described above for the reciprocal hydrogenation reactions of amides to alcohols and amines. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (FIG. 1A).

In some embodiments, beta-amino alcohols can be dehydrogenated in the presence of Ruthenium complexes to form cyclic dipeptides. Such reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (for complex F preferably L_4 is $CH_2NR^aR^b$), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Alternatively, such reactions can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes in which L_1 is $N(R)_2$, as described above for the reciprocal hydrogenation reactions of amides to alcohols and amines.

Preparation of polypeptides or cyclic peptides by dehydrogenation of beta-amino alcohols, catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, namely compounds A1', A2' or A3' in which L_1 is $N(R)_2$, has not previously been described, and constitutes another embodiment of the present invention.

In another embodiment, beta-amino alcohols can be dehydrogenated to form pyrazines in the presence of Ruthenium complexes. Ruthenium complexes which catalyze the dehydrogenation of beta-amino alcohols to pyrazines are those which contain two phosphnine ligands or N-heterocyclic carbene ligands. Examples of such complexes are described in US Patent publication US 2009/0112005, in particular Ruthenium complexes of Formulae A1', A2' and A3', and any Ruthenium complexes covered by such Formulae, wherein the Ruthenium complex comprises two phosphine $(P(R)_2)$ ligands or two N-heterocyclic carbene ligands:
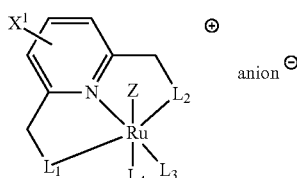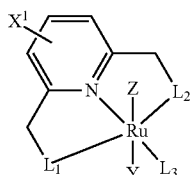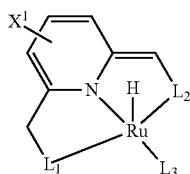
A1'

A2'

A3'

anion $\ominus$

$\oplus$

wherein

L_1 and L_2 are each independently selected from the group consisting of phosphine ($P(R)_2$), and an N-heretocyclic carbene represented by the structure:

R^3 R^2

$—N$ $N—R^3$
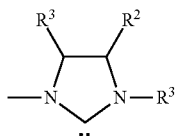
wherein each of R, R^2 and R^3 are independently selected from the group consisting of alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;

L_3 is a mono-dentate two-electron donor selected from the group consisting of CO, $P(R)_3$, $P(OR)_3$, NO^+, $As(R)_3$, $Sb(R)_3$, $S(R)_2$, nitrile (RCN) and isonitrile (RNC) wherein R is as defined above;

L_4 is absent or is L_3;

Y and Z are each independently H or an anionic ligand selected from the group consisting of halogen, OCOR, $OCOCF_3$, OSO_2R, OSO_2CF_3, CN, OH, OR, $N(R)_2$, RS and SH; wherein R is as defined above;

X represents zero, one, two or three substituents selected from the group consisting of alkyl, aryl, halogen, nitro, amide, ester, cyano, alkoxy, cycloalkyl, alkylaryl, heterocyclyl, heteroaryl, an inorganic support and a polymeric moiety;

and anion represents a group bearing a single negative charge.

Preferably the Ruthenium complex is represented by the structure of formula 2.

Other examples of such complexes include borohydride complexes represented by formula F (wherein each one of L^1 and L^4 contain a phosphine (PR^aR^b), and/or N-heterocyclic carbene), or complexes G, 2' and 6', with each possibility representing a separate embodiment of the present invention. A non-limiting example of a process for pyrazine formation is illustrated in Scheme 46 hereinbelow.

4. Dehydrogenative Coupling of Alcohols:

The present invention further provides a process for preparing esters by coupling of alcohols in the presence of a Ruthenium complex, to generate the ester compound and molecular hydrogen. In one embodiment, the process involves coupling of primary alcohols. In another embodiment, the process involves coupling of a primary and secondary alcohol. These reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Use of dialcohols in the reaction leads to polyesters or to lactones.

In one embodiment, the process of the invention, i.e., the direct catalytic coupling of primary alcohols into esters and dihydrogen is illustrated in Scheme 9A. In accordance with this process, two equivalents of a primary alcohol represented by formula $R^{13}CH_2OH$ are converted to an ester by the structure $R^{13}—C(=O)—OCH_2R^{13}$. This novel, environmentally benign reaction, can be used to produce various esters from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.

Scheme 9A

$$2\ R^{13}\diagdown OH \longrightarrow R^{13}\diagup C(=O)—O\diagdown R^{13} \quad + \quad 2H_2$$
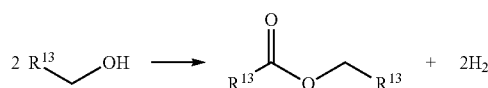
In another embodiment, the process of the invention involves the catalytic coupling of a primary alcohol and a secondary alcohol, as illustrated in Scheme 9B.

Scheme 9B
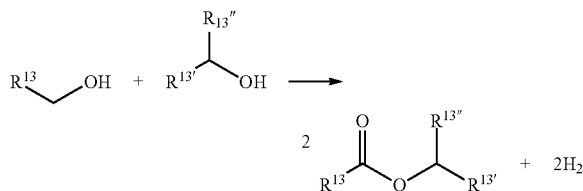
$$R^{13}\diagdown OH \ + \ R^{13'}\diagup \substack{R_{13}'' \\ }OH \longrightarrow$$

$$2 \quad R^{13}\diagup\substack{O\\\|}\diagdown O\diagup\substack{R^{13''}\\R^{13'}} \quad + \quad 2H_2$$

wherein R^{13}, $R^{13'}$ and $R^{13''}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

When primary alcohols are used, the process of the invention contemplates symmetric coupling of alcohols to yield symmetric esters (i.e., 2 equivalents of the same alcohol are coupled). However, the present invention further contemplates the generation of asymmetric esters by coupling of different alcohols. In accordance with this embodiment, a first primary alcohol represented by formula $R^{13}CH_2OH$ is reacted with a second alcohol represented by formula $R^{13'}CH_2OH$ so as to generate an ester by the structure $R^{13}—C(=O)—OCH_2R^{13'}$ or an ester of formula $R^{13'}—C(=O)—OCH_2R^{13}$, as illustrated in Scheme 10:
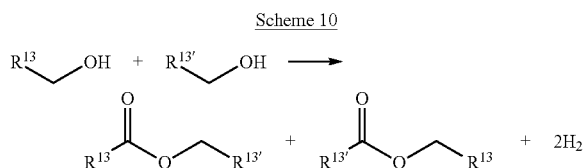
Scheme 10

wherein R^{13} and $R^{13'}$ are the same or different from each other and are each independently selected is from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, 2-methyl-1-butanol, benzyl alcohol, 1-phenylethanol and cyclohexane methanol. Each possibility represents a separate embodiment of the present invention.

In another embodiment, the process of the invention can also be applied to bis-acylation reactions with dialcohols to yield polyesters.

The reaction between the alcohols can be inter-molecular (i.e., the two alcohols are separate molecules). Alternatively, the reaction between the alcohols can be intra-molecular, i.e., the alcohol functionalities can be present in the same molecule, resulting in intra-molecular cyclization to generate a lactone. In some embodiments, the intra-molecular dehydrogenation of diols to generate a lactone is catalyzed by borohydride Ruthenium complexes as described herein, for example compounds D, E, F, G, H, 2', 4', 6' and 8'. In some embodiments, the complex is a Ruthenium complex of formula 2'. In other embodiment, the complex is a Ruthenium complex of formula 4'. Each possibility represents a separate embodiment of the present invention.

5. Dehydrogenation of Secondary Alcohols:

The present invention further relates to a process for preparing a ketone by dehydrogenation of a secondary alcohol, comprising the step of reacting the secondary alcohol in the presence of the Ruthenium complex which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae, thereby generating the ketone and molecular hydrogen.

The process of the invention, i.e., the direct catalytic conversion of secondary alcohols into ketones and dihydrogen is illustrated in Scheme 11A. In accordance with this process, a secondary alcohol represented by formula $R^{14}CH(OH)R^{14'}$ is converted to a ketone represented by the structure R^{14}—C(=O)—$R^{14'}$:
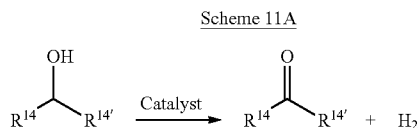
Scheme 11A

A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of 1-phenyl-1-ethanol, 2-hexanol, cyclohexanol and 2-propanol. Each possibility represents a separate embodiment of the present invention.

6. Synthesis of Amides from Esters and Alcohols

The present invention further provides a process for preparing amides, by reacting an amine and an ester in the presence of a Ruthenium complex, to generate the amide compound and molecular hydrogen (H_2). As contemplated herein, the inventors have further discovered a novel process for preparing amides in which primary and secondary amines are directly reacted with esters to produce amides and molecular hydrogen in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (when complex F is used and L^4 is —CH_2-L^1, L^1 is preferably NR^aR^b), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Reactions of esters with diamines leads to diamides.

The process of the invention, i.e., the direct catalytic reaction of esters and amines into amides and dihydrogen is illustrated in Scheme 11B. In accordance with this process, an amine represented by formula $R^{15}R^{15'}NH$ is reacted with an ester represented by the formula R^{16}—C(=O)—$OCH_2R^{16'}$ to generate an amide represented by the structure R^{16}—C(=O)—$NR^{15}R^{15'}$. This novel, environmentally benign reaction can be used to produce various amides from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.

Scheme 11B
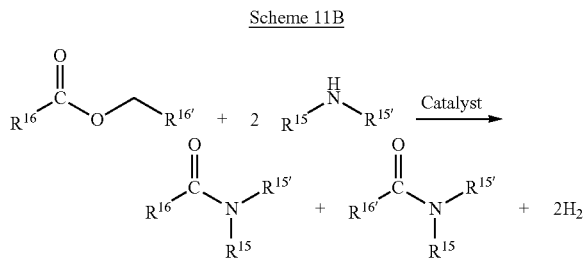
wherein R^{15}, $R^{15'}$, R^{16} and $R^{16'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein R^{15}, $R^{15'}$ and R^{16} can be the same or different from each other.

A variety of esters can be used in the process of the invention. In some embodiments, the ester is selected from the group consisting of ethyl acetate, butyl butyrate, pentyl pentanoate and hexyl hexanoate. Each possibility represents a separate embodiment of the present invention.

A variety of primary and secondary amines (as well as ammonia) may be used in the process of the invention. In some embodiments, the amine is selected from the group consisting of pyrrolidine, morpholine, 1-methyl piperazine, piperidine, piperazine, 1-hexylamine and p-tolylmethanamine.

In another embodiment, the process of the invention can also be applied to bis-acylation reactions with diamines. Upon reacting alcohols and diamines, the corresponding bis-amides are produced in high yields.

7. Acylation of Alcohols Using Esters with Liberation of H_2

The present invention further provides a process for preparing esters by acylation of alcohols using esters in the

presence of a Ruthenium complex, to generate the ester compound and molecular hydrogen. In one embodiment, the process involves reaction of primary alcohols and esters. In another embodiment, the process involves reaction of a secondary alcohols and esters. These reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

In one embodiment, the process of the invention, i.e., the direct catalytic acylation of alcohols using esters to yield an ester and dihydrogen is illustrated in Scheme 12A. In accordance with this process, two equivalents of a primary or secondary alcohol represented by formula $R^{17}R^{17'}CHOH$ reacts with one equivalent an ester by the structure R^{18}—C(=O)—OCH_2R^{18} as shown in Scheme 12A. This novel, environmentally benign reaction, can be used to produce various esters from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.

Scheme 12A
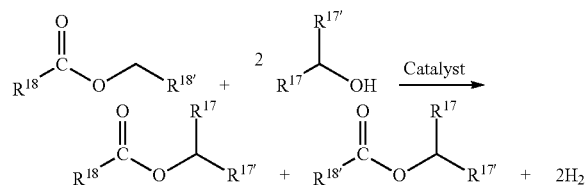
wherein R^{17}, $R^{17'}$, R^{18} and $R^{18'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of cyclohexanol, cyclopentanol, 1-phenylethanol, isopropanol and 3-pentanol. Each possibility represents a separate embodiment of the present invention.

A variety of esters can be used as the starting materials. In some embodiments, the ester is selected from the group consisting of ethyl acetate, hexyl hexanoate, pentyl pentanoate, butyl butyrate, ethyl butyrate and methyl hexanoate.

8. Coupling of Alcohols with Water to Form Carboxylic Acid with Liberation of H_2

The present invention further provides a process for preparing carboxylic acids by contacting primary alcohols with water in the presence of a Ruthenium complex and a base, to generate the carboxylic acid salt and molecular hydrogen and, if desired, followed by conversion of the carboxylic acid salt to the corresponding carboxylic acid. These reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. This reaction can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, such as, but not limited to compounds of formulae A 1', A2' and A3':
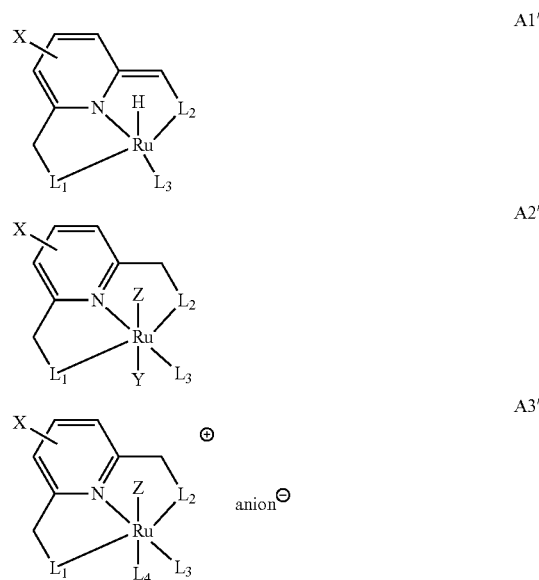
wherein
L_1 and L_2 are each independently selected from the group consisting of nucleophilic carbene (:C(R)$_2$), P(R)$_2$, P(OR)$_2$, N(R)$_2$, imine, SR, SH, S(=O)R, heteroaryl wherein the heteroatom is selected from nitrogen and sulfur, As(R)$_2$, Sb(R)$_2$ and an N-heretocyclic carbene represented by the structure:
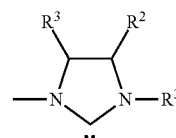
each of R, R^2 and R^3 are independently selected from the group consisting of alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
L_3 is a mono-dentate two-electron donor selected from the group consisting of CO, P(R)$_3$, P(OR)$_3$, NO$^+$, As(R)$_3$, Sb(R)$_3$, S(R)$_2$, nitrite (RCN) and isonitrile (RNC) wherein R is as defined above;
L_4 is absent or is L_3;
Y and Z are each independently H or an anionic ligand selected from the group consisting of halogen, OCOR, OCOCF$_3$, OSO$_2$R, OSO$_2$CF$_3$, CN, OH, OR, N(R)$_2$, RS and SH; wherein R is as defined above;
X represents zero, one, two or three substituents selected from the group consisting of alkyl, aryl, halogen, nitro, amide, ester, cyano, alkoxy, cycloalkyl, alkylaryl, heterocyclyl, heteroaryl, an inorganic support and a polymeric moiety; and
anion represents a group bearing a single negative charge.

Preferred complexes for this reaction are Pincer complexes represented by the structure of Formula 1.

In one embodiment, the process of the invention, i.e., the direct catalytic conversion of primary alcohols to carboxylic acids and dihydrogen is illustrated in Scheme 12B. In accordance with this process, a primary alcohol represented by formula $R^{17}CH_2OH$ is contacted with water and a base (e.g., NaOH) as shown in Scheme 12B. This novel, environmentally benign reaction, can be used to produce various carboxy-

lic acids and their salts from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste. If desired, the salt is neutralized with the appropriate acid to provide the corresponding carboxylic acid.

Scheme 12B
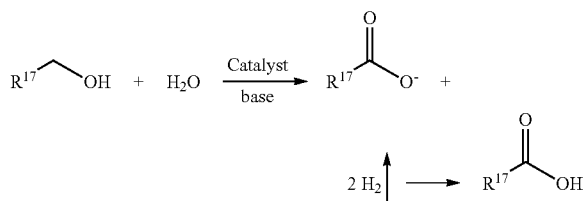
$$R^{17}\diagup\diagdown OH + H_2O \xrightarrow[\text{base}]{\text{Catalyst}} R^{17}\diagdown\underset{O}{\overset{O}{\parallel}}O^- +$$

$$2 H_2 \longrightarrow R^{17}\underset{O}{\overset{O}{\parallel}}OH$$

wherein R^{17} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

A variety of bases can be used for this reaction, non-limiting examples of which include an inorganic or organic base selected from sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide, sodium ethoxide, potassium tert-butoxide, sodium methoxide. The acid used to neutralize the salt can be, e.g. a mineral acid such as hydrochloric acid, hydrobromic acid, and the like. Each possibility represents a separate embodiment of the invention.

A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of butanol, pentanol, decanol, 2-methoxyethanol, 2-phenylethanol, cyclohexylmethanol, 3-phenylbutan-1-ol, but-3-en-1-ol, (4-methoxyphenyl)methanol, and (2,4-dimethoxyphenyl)methanol. Each possibility represents a separate embodiment of the present invention.

The disclosures of all cited references are incorporated by reference as if fully set forth herein.

The principles of the present invention are demonstrated by means of the following non-limiting processes.

EXAMPLES

Example 1

Hydrogenation of Amides to the Corresponding Alcohols and Amines

Examples of processes involving the hydrogenation of amides to alcohol and amines are shown in Scheme 13:

Scheme 13

$$R\underset{O}{\overset{O}{\parallel}}\underset{\underset{H}{N}}{}R' + 2 H_2 \xrightarrow[\text{THF, }110^\circ\text{ C.}]{\text{Catalyst (1mol \%)}} R\overset{H}{\underset{OH}{\overset{H}{\diagup}}} +$$

$$R'\!-\!\underset{\underset{H}{}}{\overset{H}{N}}$$
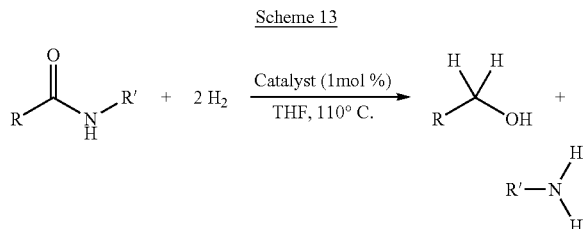
R, R' = H, Aryl, alkyl, Aryalkyl, etc.

(a) Using Catalyst 3:

A 100 mL Fischer-Porter tube was charged under nitrogen with the catalyst 3 (0.01 mmol), an amide (1.0 mmol), and

THF (2 mL). The nitrogen present in the Fischer-Porter (100 mL) was replaced by H_2 (twice with 30 psi) at room temperature, then it was filled with H_2 (10 atm). The solution was heated at 110° C. (bath temperature) with stirring for 48 hrs. After cooling to room temperature, the H_2 was vented carefully and the products were determined by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

(b) Using Complex 4+Base (Generation of Catalyst 3 In Situ):

In an open air, a solution of amide (1.0 mmol) in THF (1.0 mL) was transferred via syringe into a Fischer-Porter tube (100 mL) contains 0.01 mmol of catalyst 4. Then, KO^{t}Bu (0.01 mmol) in THF (1.0 mL) was added and the air present in the Fischer-Porter tube was flushed with hydrogen (thrice with 30 psi) and filled with H_2 (10 atm). The solution was heated at 110° C. (bath temperature) with stirring for 48 hrs. After cooling to room temperature, the H_2 was vented carefully and the products were determined by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Results of some typical processes are shown in Tables 1A, 1B and 2.

A. Selective Hydrogenation of Amides to Alcohols and Amines Using H_2 catalyzed by BPy-PNN—Ru(II) Pincer Complexes 1, 4 and 7

TABLE 1A

Hydrogenation of amides catalyzed by complex 1, 4 and 7

Reaction condition[a]

Scheme 13
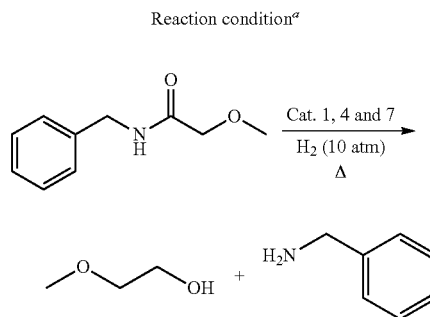
En-try	Cata-lyst	Yield (%)[b]	
		Alcohol	Amine
1	1	62.7	62.0
2	1	66.3	66.8[c]
3	4	—	—
4	4 + KO^{t}Bu	80.2	81.8[d]
5	7 + KO^{t}Bu	76.8	78.0[d]

[a]Complex 1, 4 and 7 (0.01 mol), amide (1 mmol), H_2 (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 100° C. (bath temperature) for 48 h.

[b]Yields of products were analyzed by GC (m-xylene as internal standard).

[c]1,4-dioxane (2 mL) at 140° C. after 48 h.

[d]one equivalent (relative to Ru) of base was used.

TABLE 1B

Hydrogenation of amides to alcohols and amines selectively catalyzed by pincer complex 3[a]

Entry	Amide	Products (yield [%])[b]	
		Alcohol	Amine
1		(89.2)	(89.6)
2		(90.7)	(90.3)
3		(73.6)	(73.9)
4		(68.8)	(68.1)
5		(56.8)	(57.3)
6		EtOH (71.0)	EtNH$_2$[c]
7		(68.4)	MeNH$_2$[c]
8		(88.0)	(87.3)
9		EtOH (94.1)	(94.9)[d]
10		(92.1)	(92.0)

TABLE 1B-continued
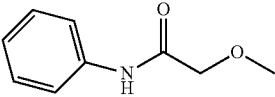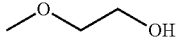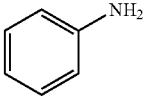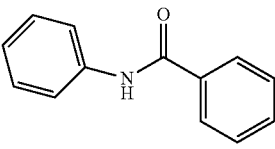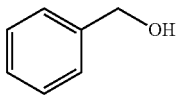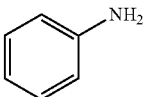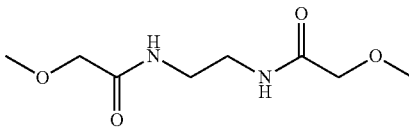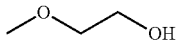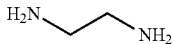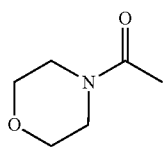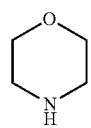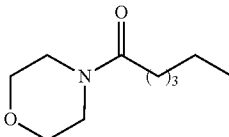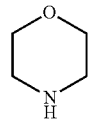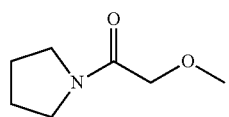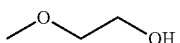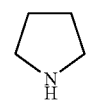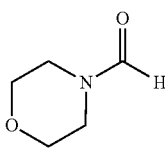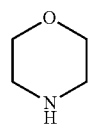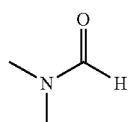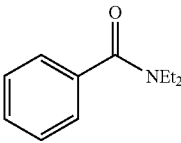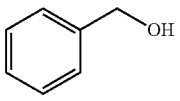
Hydrogenation of amides to alcohols and amines selectively catalyzed by pincer complex 3[a]

Entry	Amide	Products (yield [%])[b]	
		Alcohol	Amine
11		(95.3)	(94.6)
12		(91.6)	(91.0)
13		(78.0)	(76.9)[e]
14		EtOH (97.1)	(98.0)
15		(95.8)	(95.7)
16		(97.0)	(97.4)
17		MeOH (97.1)	(98.3)[f]
18		MeOH (96.3) (32.1)[g]	Me₂NH

TABLE 1B-continued

Hydrogenation of amides to alcohols and amines selectively catalyzed by pincer complex 3[a]

		Products (yield [%])[b]	
Entry	Amide	Alcohol	Amine
19			EtNH$_2$[c]

[a]Complex 3 (0.01 mol), amide (1 mmol), H$_2$ (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110° C. (bath temperature) for 48 h.
[b]Yields of products were analyzed by GC (m-xylene as internal standard).
[c]The amines (EtNH$_2$ (entry 6 and 18) and MeNH$_2$ (entry 7)) were analyzed in the gas phase by GC-MS.
[d]In the reactions involving anilide derivatives (entries 9-12), trace amounts of the corresponding secondary amines were detected by GC-MS.
[e]0.5 mmol of bis-amide was used.
[f]Yield after 32 h.
[g]Complex 1 was used.

B. Selective Hydrogenation of Primary Amides to Alcohols and Ammonia Using H$_2$ Catalyzed by Ruthenium Pincer Complex 3
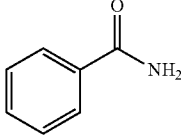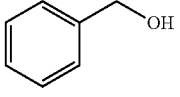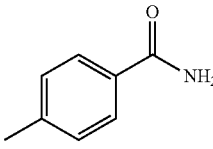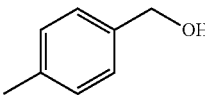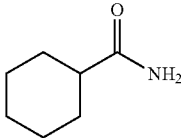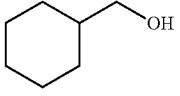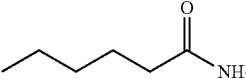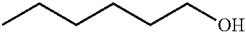
Scheme 14

$$R\overset{O}{\underset{}{\|}}{-}NH_2 \ + \ 2\,H_2 \quad \xrightarrow[\text{THF, }110°\text{ C.}]{\text{Cat. 3 (1 mol \%)}} \quad R{-}CH_2{-}OH \ + \ NH_3$$

10 atm

R = Aryl, alkyl, and vinyl

TABLE 2

Hydrogenation of primary amides to alcohols and ammonia selectively catalyzed by complex 3

Entry	Amides	Alcohols	Yield (%)[b]
1			86.8 (63.7)[c,d]
2			88.1[d]
3			90.7[d]
4			89.1 (91.7)[d,e]

TABLE 2-continued

Hydrogenation of primary amides to alcohols and ammonia selectively catalyzed by complex 3

Entry	Amides	Alcohols	Yield (%)[b]
5	O ⫿ NH₂	OH	92.5[d]
6	O ⫿ NH₂	OH	95.7
7	O ⫿ NH₂	OH	42.4

[a]Complex 3 (0.01 mol), amide (1 mmol), H₂ (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110° C. (bath temperature) for 72 h.
[b]Yields of products were analyzed by GC (m-xylene as internal standard) and ammonia was analyzed in the gas phase by GC-MS.
[c]Yield in the parenthesis after 48 h.
[d]Traces of corresponding esters were also observed in GC.
[e]1,4-dioxane (2 mL) at 140° C. after 60 h.

Discussion:

The applicants have previously reported the dehydrogenative coupling of alcohols with amines to form amides, catalyzed by complex 1, with liberation of hydrogen gas (Gunanathan 2007). To explore whether it might be possible to reverse this reaction by the application of hydrogen pressure, complexes 1-4 were tested as catalysts for the hydrogenation of amides. Thus, upon treatment of N-benzyl-2-methoxyacetamide with dihydrogen (10 atm) at 110° C. (bath temperature) in dry THF for 48 h with a catalytic amount of 1 (1 mol %), 62.7% of 2-methoxyethanol and 62.0% of benzyl amine were obtained. Performing the reaction at 140° C. using 1,4-dioxane as solvent did not significantly improve the yield (alcohol yield 66.3%). It was significant that the reaction was selective and the corresponding secondary amine was not observed. Under the same conditions complex 2 was inactive. Remarkably, employing complex 3 (1 mol %) as catalyst, hydrogenation of N-benzyl-2-methoxyacetamide under identical conditions (THF, 110° C.) resulted in the selective formation of 89.2% 2-methoxyethanol and 89.6% benzyl amine (Table 1B, entry 1). Thus, the normally observed C—O hydrogenolysis did not take place at all. Of practical significance, the air-stable complex 4 (which is stable in air for at least two days in solution) in the presence of one equivalent (relative to Ru) of base also efficiently catalyzes the hydrogenation of amides to alcohols and amines, by generation of the catalyst 3 in situ. Thus, upon heating a THF solution of 4 (1 mol %) with KO'Bu (1 mol %) and N-benzyl-2-methoxyacetamide (1 mmol) at 110° C. under H₂ (10 atm) for 48 h, 80.2% of alcohol and 81.8% of amine were formed. No reaction took place in the absence of base. Hydrogenation of N-hexyl-2-methoxyacetamide catalyzed by 3 yielded 2-methoxy ethanol and hexyl amine in 90.7% and 90.3% yields, respectively (Table 1B, entry 2). N-hexyl-3-methyloxetane-3-carboxamide undergoes hydrogenation to the alcohol and amine without hydrogenolysis of the strained oxetane ring (Table 1B, entry 3). The heterocyclic amide, N-hexylfuran-2-carboxamide was hydrogenated to yield 68.8% of furfuryl alcohol and 68.1% of hexylamine (Table 1B, entry 4). The aromatic non-activated amide, N-benzylbenzamide is also hydrogenated to benzyl alcohol and benzyl amine (Table

1B, entry 5), but the yield is lower, probably because of steric reasons. Significantly, the aliphatic non-activated amides, N-ethylacetamide and N-methylpropionamide also underwent hydrogenation to yield the corresponding alcohols and amines (71% of ethanol and ethylamine for entry 6 and 68.4% of n-propanol and methylamine for entry 7). The product gaseous amines were analyzed by GC-MS spectrometry of the gas phase and not quantified. As expected, the activated amides, anilide derivatives, were converted into their corresponding alcohols and aniline in excellent yields (91-95%; Table 1B, entries 9-12) along with trace amounts of the secondary amines (detected by GC-MS) under similar conditions. The reaction is also effective for bis-amides. Thus, N,N'-(ethane-1,2-diyl)bis(2-methoxyacetamide) (0.5 mmol) was also hydrogenated using catalyst 3 under mild conditions (Table 1B, entry 13). Noteworthy, tent-amides also underwent hydrogenation almost quantitatively to yield alcohols and secondary amines in equivalent amounts (Table 1B, entries 14-16). Gratifyingly, heating a solution of N-formyl-morpholine (1 mmol) and complex 3 in THF at 110° C. yielded after 32 h 97.1% of methanol and 98.3% of morpholine; no decarbonylation of the formyl group took place (Table 1B, entry 17). These results highlight the substantial scope of the unprecedented, selective hydrogenation of amides catalyzed by 3, or by the air-stable 4 with an equivalent of base (which generates 3 in situ).

In conclusion, amides can be selectively hydrogenated to alcohols and amines for the first time. The reaction proceeds under mild pressure, neutral, homogeneous conditions using Ruthenium complexes as catalysts according to the invention and dihydrogen by metal-ligand cooperation. This new catalytic protocol exhibits a broad substrate scope providing a variety of amines and alcohols in good to excellent yield.
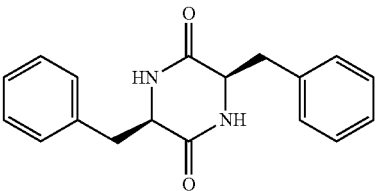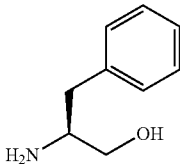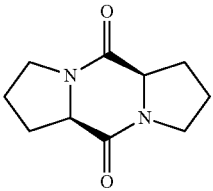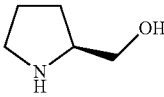
C. Hydrogenation of Cyclic Di-Peptides

The process of the present invention can also be used for catalytic hydrogenation of di-peptides. For example, cyclic di-peptides can be hydrogenated to amino alcohols. In a general procedure, a 100 mL Fischer-Porter tube was charged with the catalyst 1 (0.02 mmol), the cyclic di-peptides (1.0 mmol) and THF (2 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure

tube was taken out of the glove box, and subjected to three successive cycles of pressurization/venting with H_2 (3 atm), then pressurized with H_2 (12 atm) and closed. The tube was placed behind a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 60 h. After cooling to room temperature, excess H_2 was vented off carefully and the product was determined by GC and GC-MS. Some representative results are presented in Table 3 hereinbelow.

Scheme 15

TABLE 3

	Hydrogenation of cyclic di-peptides to amino alcohols selectively catalyzed by complex 1		
Entry	Cyclic di-peptides	Conditions	Amino alcohols (Yield (%))
1		Solvent = THF (2 mL) PH_2 = 10 atm Temperature = 110° C. (bath) Time = 60 h	(58%)
2			(67%)

Example 2

Hydrogenation of Formate Esters to Methanol and Alcohols; Dimethyl Carbonate to Methanol; Esters and Lactones to Alcohols, and Hydrogenation of Polycarbonates

A. Hydrogenation of Formates/Carbonate:

A 100 mL Fischer-Porter tube was charged under nitrogen with catalyst 3 (0.01 mmol), formate ester (15.0 mmol) or dimethyl carbonate (10.0 mmol) and THF (2 mL). After the nitrogen present in the Fischer-Porter tube was replaced by H_2 (twice with 30 psi) at room temperature, the tube was filled with H_2 (10 atm). The solution was heated at 110° C. (bath temperature) with stirring for 36 hrs. After cooling to room temperature, excess H_2 was vented carefully and the products were analyzed by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

B. Hydrogenation of Methyl Formate and Dimethyl Carbonate Under 50 Atmospheres and Very Low Catalyst Loading (Entries 6 and 10, Respectively, Table 4):

A 30 mL Teflon coated Iron-Fischer-Porter (Autoclave) was charged under nitrogen with catalyst 3 (0.005 mmol), Methyl Formate (25.0 mmol) and THF (5 mL). After the nitrogen present in the autoclave was replaced by H_2 (twice with 50 psi) at room temperature, it was filled with H_2 (40 atm). The solution was heated at 110° C. (bath temperature) with stirring for 14 hrs. After cooling to room temperature, the H_2 was vented carefully at 0° C. and the products were determined by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system. The same procedure was used for hydrogenation of dimethyl carbonate.
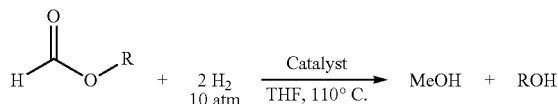
-continued
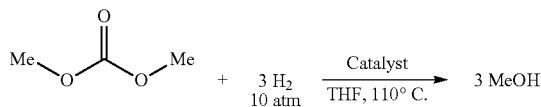
TABLE 4

	Hydrogenation of Formates[a] and Dimethyl Carbonate[b]				
Entry	Catalyst	Substrate	Conv. (%)	Products (%)[c]	TON
1	1	HCOOMe (MF)	71.7	71.0[d]	710
2	1	HCOOMe	>99	~99[e]	990
3	1	HCOOMe	78.3	2 MeOH (77.0)[a]	1155
4	3	HCOOMe	96.0	2 MeOH (95.8)	1440
5	7 + KOtBu	HCOOMe	92.8	2 MeOH (91.2)[f]	1370
6	3	HCOOMe	94.0	2 MeOH (93.7)[g]	4685
7	3	HCOOEt	92.0	MeOH (92.0) and EtOH (91.7)	1380
8	3	HCOOnBu	86.3	MeOH (86.3) and n-BuOH (86.0)	1295
9	3	DMC	96.2	3 MeOH (96.2)	962
10	3	DMC	89.0	3 MeOH (87.6)[g]	4380

[a]Complex 1 or 3 (0.01 mmol), formate (15 mmol), H_2 (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110° C. (bath temperature) for 48 h.
[b]10 mmol of DMC was used.
[c]Yields of products and conversion of starting material were analyzed by GC (m-xylene as internal standard).
[d]100 psi H_2, 1,4-dioxane (2 mL) at 145° C. after 30 h.
[e]130 psi H_2, 1,4-dioxane (2 mL) at 145° C. after 36 h.
[f]one equivalent (relative to Ru) of base was used.
[g]Complex 3 (0.005 mmol), MF/DMC (25 mmol), H_2 (50 atm), and dry THF (5 ml) were heated in a autoclave at 110° C. (bath temperature) for 14 h.

C. Hydrogenation of Methyl Formate and Dimethyl Carbonate Under Neat Conditions

A 100 mL Fischer-Porter tube was charged under nitrogen with catalyst 3 (0.01 mmol), and methyl formate or dimethyl carbonate (10.0 mmol). After the nitrogen in the Fischer-Porter tube was replaced by H_2 (twice with 30 psi) at 0° C., the tube was filled with H_2 (10 atm). The solution was heated at 80° C. (for MF) and 100° C. (for DMC) (bath temperature) with stirring for 8 hrs. After cooling to room temperature, excess H_2 was vented carefully and the products were analyzed by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Scheme 16
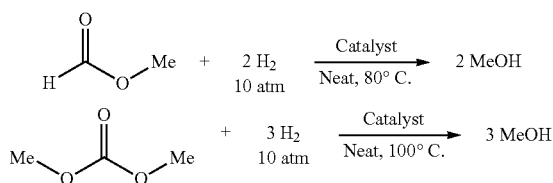
TABLE 5

Hydrogenation of methyl formate and dimethyl carbonate

Entry	Catalyst	Substrate	Conv. (%)	Products (%)[a]
1	1	HCOOMe	15.6	2 MeOH (15.2)[b]
2	3	HCOOMe	>99	2 MeOH (>99)[c]
3	3	DMC	>99	3 MeOH (>99)[d] (89.1)[e]

[a]Yields of product and conversion of starting material were analyzed by GC (m-xylene as internal standard).
[b]Complex 3 or 1 (0.01 mol), formate (10 mmol), and H_2 (10 atm) were heated in a Fischer-Porter tube at 80° C. (bath temperature) for 18 h.
[c]10 mmol of DMC was used.
[c]Yields after 8 h.
[d]at 100° C. after 8 h.
[e]at 100° C. after 2 h.

D. Hydrogenation of Carbamates:[a]

TABLE 6

hydrogenation of carbamates to amines and alcohols

Entry	Carbamate	Alcohol	Amine	Yield[b]
1		2 MeOH		97.8
2		2 MeOH		98.0

[a]Complex 3 (0.01 mol), carbamate (1 mmol), and H_2 (10 atm) were heated in a Fischer-Porter tube a 110° C. (bath temperature) for 48 h.
[b]Yields of product (based on MeOH) were analyzed by GC (m-xylene as internal standard).

E. Hydrogenation of Unactivated Esters (Hexyl Hexanoate):

A 30 mL Teflon coated Iron-Fischer-Porter (Autoclave) was charged under nitrogen with catalyst 3 (0.01 mmol for entry 1 and 0.005 mmol for entry 2 respectively), hexyl hexanoate (20.0 mmol) and THF (5 mL). After the nitrogen present in the autoclave was replaced by H_2 (twice with 50

psi) at room temperature, it was filled with H_2 (50 atm). The solution was heated at 110° C. (bath temperature) with stirring for 16 hrs. After cooling to room temperature, the H_2 was vented carefully and the yields of product and conversion of starting material were analyzed by GC (m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system. Very high turnover numbers (TON) were obtained.

Scheme 17
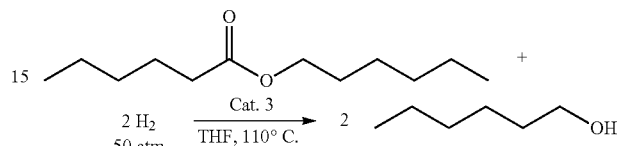
TABLE 7

Hydrogenation of esters to alcohols

Entry	Cat.	Ester	Alcohol (20 mmol)	Yield (%)	TON
1	3 (0.01 mmol)	Hexyl hexanoate	1-Hexanol	>99	2000
2	3 (0.005 mmol)	Hexyl hexanoate	1-Hexanol	82.1	3284

F. Hydrogenation of Biomass-Derived Cyclic Di-Esters to 1,2-Diols

The cyclic di-ester of glycolic acid (derived from sugar cane), glycolide was chosen as a model substrate for catalytic hydrogenation by Ruthenium complex 3. A 1,4-dioxane solution containing glycolide (1 mmol) and 1 mol % of complex 3 was heated under hydrogen pressure (6 atm) at 135° C. for 36 h using a pressure vessel. The reaction mixture was cooled and excess H_2 was vented carefully and the products were determined by GC and GC-MS showing formation of ethylene glycol (EG) as the only product in 61% yield (Table 8, entry 1) with 67% conversion of the glycolide. After removal of the solvent, the obtained crude viscous liquid was further analyzed by ESI, illustrating that there was no formation of polymeric material.

Performing the same reaction under similar conditions using 10 atm of H_2 resulted in 88% of ethylene glycol after 36

h (Table 8, entry 2). Optimization studies revealed that the reaction could be performed at lower temperature using THF as solvent. Thus, heating complex 3 (0.01 mmol) with glycolide (1 mmol) and dihydrogen (10 atm) at 110° C. in 3 mL of dry THF for 48 h using a Fisher-Porter tube, yielded 93% of ethylene glycol (Table 8, entry 3). A high turnover number (425) was achieved at higher pressure. Thus, heating a THF solution of glycolide (10 mmol) and a catalytic amount of complex 3 (0.02 mmol) at 110° C. under H_2 (50 atm) using a high pressure reactor resulted in 85% yield of ethylene glycol selectively after 12 h (Table 8, entry 4).

Scheme 18

not observed
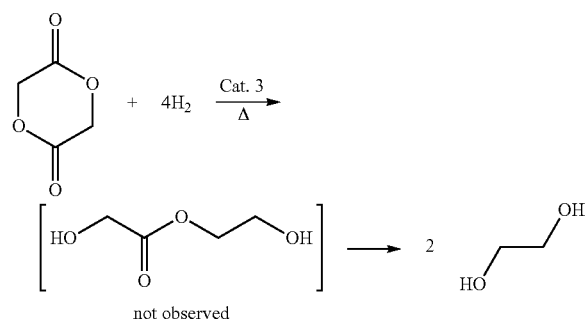
TABLE 8

Catalytic hydrogenation of glycolide to ethylene glycol

entry	solvent	temp. (° C.)	P(H_2) (atm)	time (h)	yield (%)[b]
1	1,4-dioxane	135	6	36	61
2	1,4-dioxane	135	10	36	88
3	THF	110	10	48	93
4[c]	THF	110	50	12	85

[a]Complex 3 (0.01 mmol), glycolide (1 mmol), H_2 and dry solvent (3 mL) were heated in a Fischer-Porter bute at the specified (oil bath) temperature.
[b]Yields of ethylene glycol were analyzed by GC using m-xylene as an internal standard.
[c]Complex 3 (0.02 mmol), glycolide (10 mmol), and THF (5 mL) were heated under H_2 pressure in a high-pressure reactor.

To expand the scope of this efficient hydrogenation reaction, optimized catalytic conditions were further tested with lactide, which is derived from the glucose fermentation product lactic acid. Thus, meso-lactide was heated with H_2 (10 atm) at 110° C. in THF for 48 h with a catalytic amount of 3 (1 mol %), 87% of 1,2-propanediol was obtained selectively (Table 9, entry 1). Remarkably, the hydrogenation of chiral lactide, L-lactide catalyzed by complex 3 under the optimized conditions yielded optically pure (S)-(+)-1,2-propanediol as sole product without racemization even under high pressure. Hence, upon treatment of L-lactide (10 mmol) with dihydrogen (50 atm) at 135° C. for 12 h with a catalytic amount of 3 (0.02 mmol) using 5 mL of THF as a solvent, selectively yielded 91% to propylene glycol (Table 9, entry 3). After careful removal of the solvent under reduced pressure, the reaction mixture was passed through short silica gel bed and

the diol was eluted with CH_2Cl_2:MeOH (10:1) and concentrated under vacuum to yield 73% of the optically pure 1,2-propanediol. The optical rotation of the pure product was essentially the same as reported in the literature. Thus, under these experimental condition, no racemization took place.

Scheme 19
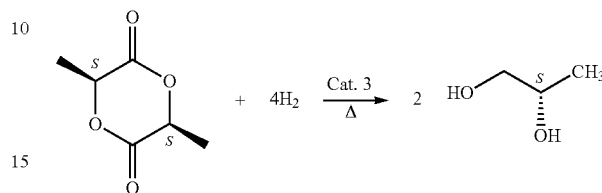
TABLE 9

Catalytic hydrogenation of lactide to propylene glycol

Entry	di-ester (lactide)	solvent	temp (° C.)	P(H_2) (atm)	time (h)	yield (%)[b]
1	meso	THF	110	10	48	87
2	chiral (S,S)	THF	110	10	48	82
3[c]	chiral (S,S)	THF	110	50	12	91(73)[d]

[a] Complex 3 (0.01 mmol), meso or chiral lactide (1 mmol), H_2, and dry THF (3 mL) were heated in a Fischer-Porter tube at 110° C. (oil bath) temperature.
[b]Yields of propylene glycol were analyzed by GC using m-xylene as an internal standard.
[c]Complex 3 (0.02 mmol), L-lactide (10 mmol), and THF (5 mL) were heated under H_2 pressure in a high-pressure reactor.
[d]Isolated yield.

In conclusion, cyclic di-esters such as glycolide and lactide are selectively hydrogenated to the corresponding 1,2-diols for the first time. This offers an environmentally benign, atom economic and an alternative approach to the indirect transformation of biomass to important synthetic building blocks, propylene and ethylene glycol. The reactions proceed under mild, neutral and homogeneous conditions with minimal pressure of molecular hydrogen. Importantly, the chirality is unaffected during the hydrogenation.

General Experimental:

All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques. All solvents were reagent grade or better. All non-deuterated solvents were refluxed over sodium/benzophenone ketyl and distilled under argon atmosphere. Deuterated solvents were used as received. All solvents were degassed with argon and kept in the glove box over 4 Å molecular sieves. Most of the chemicals used in the catalytic reactions (cyclic di-esters) are commercially available and were used as received.

Thin layer chromatography (TLC) was performed using Merck 1.05554 aluminum sheets precoated with silica gel 60 F254 and the spots were visualized with UV light at 254 nm or under iodine vapor. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60 (0.063-0.200 mm).

1H, 13C and 31P NMR spectra were recorded using a Bruker AMX-300 NMR spectrometer. NMR chemical shifts are reported in ppm downfield from tetramethylsilane (for CDCl3). ^{1}H NMR chemical shift is referenced to the residual hydrogen signal of the deuterated solvent (7.15 ppm for benzene). ^{31}P NMR chemical shift is reported in ppm downfield from H_3PO_4 and referenced to an external 85% solution of

phosphoric acid in D2O. Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were recorded on a Nicolet FT-IR spectrophotometer. Mass spectra were recorded on Micromass Platform LCZ 4000, using Electro Spray Ionization (ESI) mode. GC-MS was carried out on HP 6890 (flame ionization detector and thermal conductivity detector) and HP 5973 (MS detector) instruments equipped with a 30 m column (Restek 5MS, 0.32 mm internal diameter) with a 5% phenylmethylsilicone coating (0.25 mm) and helium as carrier gas. GC analysis were carried out using a Carboxen 1000 column on a HP 690 series GC system or HP-5 cross linked 5% phenylmethylsilicone column (30 m×0.32 mm×0.25 μm film thickness, FID) on a HP 6890 series GC system using m-xylene (1 mmol) as an internal standard.

General Procedure for Catalytic Hydrogenation:

(a) Catalytic Hydrogenation of Glycolide to Ethylene Glycol:
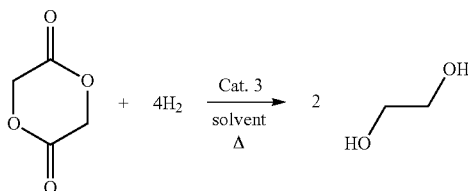
(i) Substrate/catalyst 100/1: A solution of catalyst 3 (4.5 mg, 0.01 mmol) in THF or 1,4-dioxane (1.0 mL) was transferred into a 100 mL Fischer-Porter tube followed by addition of the glycolide (116 mg, 1.0 mmol) in THF or 1,4-dioxane (2.0 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/venting with H_2 (2 atm), then pressurized with H_2 (10 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 48 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard, using a HP-5 cross linked 5% phenylmethylsilicone column (30 m×0.32 mm×0.25 μm film thickness) on a HP 6890 series GC system.

(ii) Substrate/catalyst 500/1: in a nitrogen glove box, a solution of catalyst 3 (9 mg, 0.02 mmol) in THF (5 mL) was added to a stainless-steel high pressure reactor (30 mL) equipped with a magnetic stirring bar containing 10.0 mmol (1.16 g) of the solid glycolide. The high pressure reactor was taken out of the glove box and the nitrogen present in the pressure reactor was flushed with hydrogen by two successive cycles of pressurization/venting with H_2 (5 atm), then pressurized with H_2 (50 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 12 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard. (After 3 hrs, the conversion of the glycolide was only 39%).

(Note: Complex 3 also catalyzed the dehydrogenation of ethylene glycol to glycolide and other polymeric material (poly glycolide) with liberation of H_2 after 24 hrs in 1,4-dioxane (conversion of ethylene glycol 16%) or under solvent free (neat) condition with less conversion (21%)).

(b) Catalytic Hydrogenation of Meso-Lactide to Propylene Glycol:
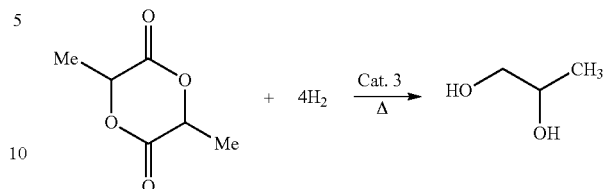
A solution of catalyst 3 (4.5 mg, 0.01 mmol) in THF (1.0 mL) was transferred into a 100 mL Fischer-Porter tube followed by addition of the meso-lactide (144 mg, 1.0 mmol) in THF (2.0 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/venting with H_2 (2 atm), then pressurized with H_2 (10 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 48 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard.

(c) Catalytic hydrogenation of L-lactide to S-(+)-1,2-propanediol:

Scheme 19
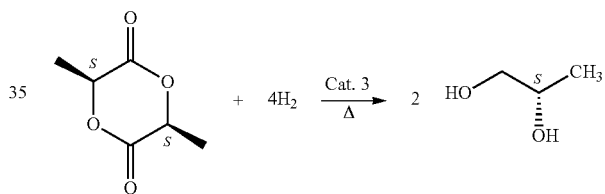
(i) Substrate/catalyst 100/1: A solution of catalyst 3 (4.5 mg, 0.01 mmol) in THF (1.0 mL) was transferred into a 100 mL Fischer-Porter tube followed by addition of L-lactide (144 mg, 1.0 mmol) in THF (2.0 mL) under an atmosphere of purified nitrogen in a glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/venting with H_2 (2 atm), then pressurized with H_2 (10 atm) and closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 48 h. After cooling to ~5° C. (with a cold water bath), excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard. After careful removal of the solvent under reduced pressure, the reaction mixture was passed through short silica gel bed and the diol was eluted with CH_2Cl_2:MeOH (10:1) and concentrated under vacuum to yield 67% of the optically pure 1,2-propanediol. The optical rotation of the pure product was essentially the same as reported in the literature.

(ii) Substrate/catalyst 500/1: in a nitrogen glove box, a solution of catalyst 3 (9 mg, 0.02 mmol) in THF (5 mL) was added to a stainless-steel high pressure reactor (30 mL) equipped with a magnetic stirring bar containing 10.0 mmol (1.44 g) of the L-lactide. The high pressure reactor was taken out of the glove box and the nitrogen present in the pressure reactor was flushed with hydrogen by two successive cycles of pressurization/venting with H_2 (5 atm), then pressurized

with H$_2$ (50 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 12 h. After cooling to ~5° C. (with a cold water bath), excess H$_2$ gas was vented carefully and the products were determined by GC with m-xylene as an internal standard. After careful removal of the solvent under reduced pressure, the reaction mixture was passed through short silica gel bed and the diol was eluted with CH$_2$Cl$_2$:MeOH (10:1) and concentrated under vacuum to yield 67% of the optically pure 1,2-propanediol. The optical rotation of the pure product was essentially the same as reported in the literature.

Hydrogenation of L-Lactide to S-(+)-1,2-Propanediol Catalyzed by NHC—Ru(II) Catalyst
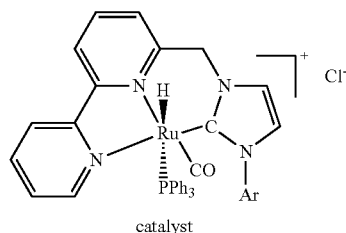
catalyst

The NHC Ru(II) pincer catalyst was prepared according to: E. Fogler, E. Balaraman, Y. Ben-David, G. Leitus, L. J. W. Shimon and D. Milstein, *Organometallics*, 2011, 30, 3826

A 100 mL Fischer-Porter tube was charged under nitrogen with the catalyst (4.5 mg, 0.01 mmol), L-lactide (144 mg, 1.0 mmol) and THF (3 mL). The Fischer-Porter tube was purged by three successive cycles of pressurization/venting with H$_2$ (2 atm), then pressurized with H$_2$ (10 atm). The solution was heated at 110° C. (bath temperature) with stirring for 48 h. After cooling to ~5° C. excess H$_2$ gas was vented and the products were determined by GC. The solvent was removed under reduced pressure and the reaction mixture was passed through short silica gel bed. The 1,2-diol was eluted with CH$_2$Cl$_2$:MeOH (10:1) and concentrated under vacuum to yield 57% of the optically pure (S)-(+)-1,2-propanediol ($[\alpha]_D^{22}$=+27° (c=1, CHCl$_3$)

G. Hydrogenation of Urea Derivatives to Amines and Methanol

Scheme 20
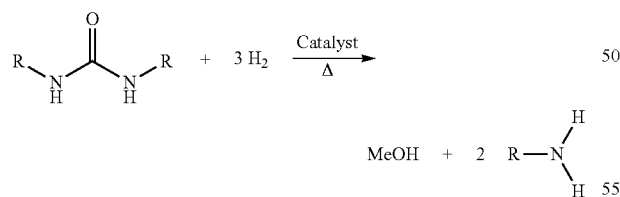
R = Aryl, alkyl, Arylalkyl, etc.

1,3-Dimethylurea was selected as a benchmark substrate for the unprecedented hydrogenation of urea derivatives catalyzed by complex 3. Upon treatment of 1,3-dimethylurea (1 mmol) and a catalytic amount of complex 3 (1 mol %) with H$_2$ (10 atm) at 110° C. (bath temperature) in dry THF resulted in 41% conversion of dimethylurea to methanol and methylamine after 48 h (Table 10, entry 1). The formed methanol was quantified as 35% by GC and the gaseous amine was characterized by GC-MS of the gas phase of the reaction

mixture and not quantified. The yield of methanol increased at longer reaction time (Table 10, entry 2). Performing the same reaction under using 13.6 atm of H$_2$ and 2 mol % of catalyst resulted in 93% of methanol after 72 h (Table 10, entry 3).

TABLE 10

Novel hydrogenation of 1,3-dimethylurea to methanol and methylamine catalyzed by 3

Entry	Cat. 3 (mol %)	PH$_2$ (atm)	hrs (atm)	Conv. (%)[b]	Yield of MeOH (%)[b],[c]
1	1	10	48	41	35
2	1	10	60	53	52
3	2	13.6	72	96	93

[a]Complex 3, 1,3-dimethylurea (1 mmol), H$_2$, and dry THF (2 mL) were heated in a Fischer-Porter tube (100 mL) at 110° C. (bath temperature) for specified time.

[b]Conversion of dimethylurea and yields of methanol were analyzed by GC using m-xylene as an internal standard.

[c]The MeNH$_2$ was analyzed in the gas phase (as well as in the liquid phase) by GC-MS and not quantified.

Various urea derivatives were subjected to hydrogenation (Table 11). Hydrogenation of 1,3-dihexylurea under the same conditions (cat/urea derivative=2:100 (mmol), 13.6 atm of H$_2$, 2 mL of dry THF, at 110° C.) yielded methanol and 1-hexylamine in 83% and 87% respectively after 72 h (Table 11, entry 2). As expected, the activated urea derivative, 1,3-bis(2-methoxyethyl)urea gave almost quantitative conversion to methanol and 2-methoxyethylamine upon hydrogenation (Table 11, entry 3). Aromatic and substituted aromatic urea derivatives also underwent hydrogenation very efficiently in moderate yields (Table 11, entries 5-7) along with trace amounts of the corresponding formamides (detected by GC-MS). The hydrogenation of diphenylurea derivatives proceeds very smoothly to yield methanol and anilines. Thus, upon heating a THF solution of 3 (0.02 mmol) and 1,3-diphenylurea (1 mmol) at 110° C. under H$_2$ (12 atm), complete conversion to selectively form 90% of methanol and 95% of aniline took place (Table 11, entry 8). Remarkably, tetra-substituted urea derivatives were also selectively hydrogenated to yield methanol and the corresponding amines, with cleavage of the C—N bond. Thus, heating a THF solution containing 1,1',3,3'-tetramethylurea (1 mmol) and a catalytic amount of the complex 3 (2 mol %) under hydrogen pressure (13.6 atm) using pressure vessel at 110° C. for 72 h resulted in 53% conversion of tetramethylurea (TMU) to methanol (51%) and N,N'-dimethylamine (Table 11, entry 11).

TABLE 11

Hydrogenation of urea derivatives to amines and methanol catalyzed by BPy-PNN-Ru(II) pincer complex 3.[a]

Entry	Amide	MeOH	Amine
1[c]		89	
2		83	(87)
3		94	(97)
4		73	(79)
5[c]		61	(60)
6[c]		67	71
7		58	59
8		90	95
9		93	87

TABLE 11-continued

Hydrogenation of urea derivatives to amines and methanol catalyzed by BPy-PNN-Ru(II) pincer complex 3.[a]

Entry	Amide	MeOH	Amine
10[c],[d]		51	(CH$_3$)$_2$NH
11[c]		63	57

R = H; R = Aryl, alkyl, and Aryalkyl
R = R' = Me and —(CH$_2$(CH$_2$)$_3$CH$_2$)—
[a]Complex 3 (0.02 mmol), urea derivative (1 mmol), H$_2$ (13.6 atm), and dry THF (2 mL) were heated in a Fischer-Porter tube (100 mL) at 110° C. (bath temperature) for 72 hrs (most of the reactions were repeated twice).
[b]Yields of products were analyzed by GC (1 mmol of m-xylene as an internal standard).
[c]The amines n-propylamine and Me$_2$NH for (entries 1 and 10 respectively) were analyzed in the gas phase (as well as in liquid phase) by GC-MS and not quantified.
[d]The corresponding formamides (entries 5-6 and 10-11) were observed on GC-MS and not quantified.

General Procedure for the Catalytic Hydrogenation of Urea Derivatives:

A 100 mL Fischer-Porter tube was charged with catalyst 3 (0.02 mmol), urea derivative (1.0 mmol) and THF (2 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box.

The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/venting with H$_2$ (3 atm), then pressurized with H$_2$ (10 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110° C. with constant stirring for 48 h. After cooling to room temperature, excess H$_2$ gas was vented carefully and the products were determined by gas chromatography (GC).

G. Hydrogenation of Polypropylene Carbonate
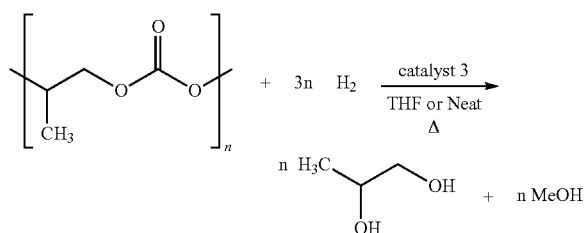
(1) A 100 mL Fischer-Porter tube was charged under nitrogen with catalyst 3 (9 mg, 0.02 mmol), polypropylene carbonate (M$_n$=50,000 by GPC; 0.255 g) and THF (2 mL). The Fischer-Porter tube was purged by three successive cycles of pressurizing/venting with H$_2$ (3 atm) and pressurized with 10 atm of H$_2$. The solution was heated at 110° C. (bath temperature) with stirring for 8 h. After cooling (~5° C.; ice/water), excess H$_2$ was vented carefully and the products were analyzed by GC-MS. The solvent was removed under vacuum to give pure 1,2-propanediol (isolated yield=0.180 g corresponds to 94.8%) and methanol (97% yield).

(2) Hydrogenation Under Solvent-Free (Neat) Conditions:

A 100 mL Fischer-Porter tube was charged with catalyst 3 (0.01 mmol) and polypropylene carbonate (M$_n$=50,000 by GPC; 0.510 g) under an atmosphere of purified nitrogen in a glovebox. The pressure tube was taken out of the glove box and purged by three successive cycles of pressurization/venting with H$_2$ (2 atm), then pressurized with H$_2$ (12.2 atm). The tube was placed behind a protective shield and heated in an oil bath at 130° C. with constant stirring for 14 h. After cooling to ~5° C., excess H$_2$ gas was vented carefully and the products (methanol and 1,2-propanediol) were analyzed by gas chromatography (GC and GC-MS) and quantified by ^{1}H NMR using toluene as internal standard. Quantitative conversion of the polymer took place, to yield 4.96 mmol of 1,2-propanediol and methanol. Isolated yield of 1,2-propanediol was 0.368 g (4.83 mmol).

Example 3

Dehydrogenatiye Coupling of Primary Alcohols to Esters

Some processes involving the coupling of alcohols to esters are shown in Scheme 21:

Scheme 21
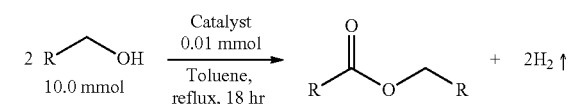
A. Typical Procedures for the Catalytic Dehydrogenative Coupling of Primary Alcohols (Table 12)

(a) Complex 3 (0.01 mmol), an alcohol (10 mmol), and toluene (2 mL) were taken in a Schlenk flask under an atmosphere

of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 24 hrs. After cooling to room temperature, the consumption of starting material and the formation of ester were determined by GC with m-xylene as an internal standard using a Carboxen 1000 column on a HP 690 series GC system.

(b) Complex 4 (0.01 mmol), an alcohol (10 mmol), KO^{t}Bu (0.01 mmol) and toluene (2 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 18 hrs. After cooling to room temperature, the consumption of starting material and the formation of ester were determined by GC with m-xylene as an internal standard using a Carboxen 1000 column on a HP 690 series GC system.

TABLE 12

Coupling of primary alcohols to form esters

Entry	Cat.	Alcohol	Ester	Conv. (%)	Yield (%)
1	4	1-Hexanol	Hexyl hexanoate	—	—
2	4 + t-BuOK	1-Hexanol	Hexyl hexanoate	95.3	95.0 + traces of aldehyde
3	7 + t-BuOK	1-Hexanol	Hexyl hexanoate	90.0	89.3 + traces of aldehyde
4	3	1-Hexanol	Hexyl hexanoate	98.6	98.2
5	3	1-Pentanol	Pentyl pentanoate	98.3	98.0
6	3	Benzyl alcohol	Benzyl benzoate	94.1	92.9 + 0.9% aldehyde
7	3	1-Butanol	Butyl butyrate	90.1	89.7 + 0.3% aldehyde
8	3	Cyclohexane methanol	Cyclohexyl-methyl cyclohexane carboxylate	98	96.2 + 1.6% aldehyde

B. Catalytic Dehydrogenation of Primary Alcohols Under Neat Condition (Absence of Solvent) (Table 13):

Complex 3 (0.01 mmol) was heated under an argon flow in different alcohols (10 mmol) at the specified temperatures and times (Table 13). After cooling to room temperature, the consumption of starting material and the formation of ester were determined by GC with m-xylene as an internal standard using a Carboxen 1000 column on a HP 690 series GC.

TABLE 13

Coupling of primary alcohols to form esters under neat conditions

Entry	Cat.	Alcohol	Temp. (° C.)	Time (hrs)	Ester	Conv. (%)	Yield (%)
1	3	1-Pentanol	138	12	Pentyl penta-noate	97.7	97.5 + traces of aldehyde
2	3	1-Butanol	117	12	Butyl butyrate	89.0	87.7 + 1.2% aldehyde
3	3	Ethanol (20 mmol)	79	72	Ethyl acetate	52.0	51.7

C. Catalytic Dehydrogenative Coupling of Alcohols Under Open Air (Table 14):

To an oven dried Schlenk flask cooled to room temperature under open air were added complex 4 (0.01 mmol), an alcohol (5 mmol) in toluene (2 mL), followed by KO^{t}Bu (0.01 mmol) in toluene (1 mL) and the flask was equipped with a condenser

and the solution was refluxed with stirring in an open system under air for 18 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with m-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

TABLE 14

Coupling of primary alcohols to form esters under open air

Entry	Alcohol	Ester	Conv. (%)	Yield (%)
1	1-Hexanol	Hexyl hexanoate	89.8	86.3 + 2.8% aldehyde
2	Benzyl alcohol	Benzyl benzoate	90.4	84.8 + 5.3% aldehyde

Example 4

Dehydrogenative Coupling of Alcohols and Amines with Liberation of H$_2$ to Form Amides

Some processes involving the coupling of alcohols and amines to generate amides are shown in Scheme 22:

Scheme 22
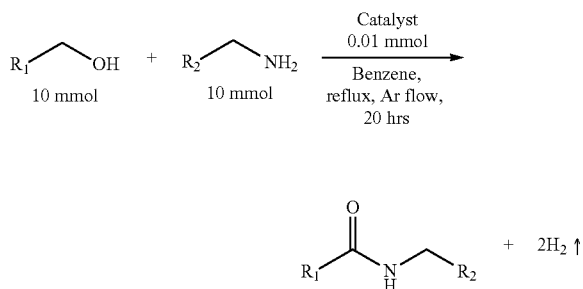
A. Typical Procedure for the Catalytic Dehydrogenative Mono-Acylation of Amines with Alcohols (Table 15):

(a) Complex 3 (0.01 mmol), an alcohol (10 mmol), an amine (10 mmol), and benzene (3 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 20 hrs. After cooling to room temperature, the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system. (b) Complex 4 (0.01 mmol), an alcohol (10 mmol), an amine (10 mmol), KO^{t}Bu (0.01 mmol), and benzene (3 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 20 hrs. After cooling to room temperature, the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system.

TABLE 15
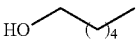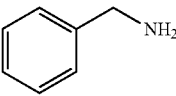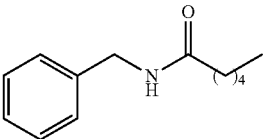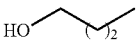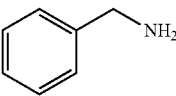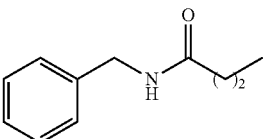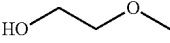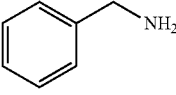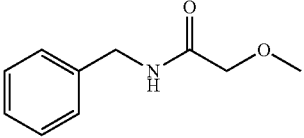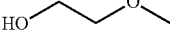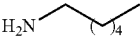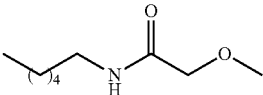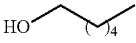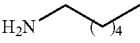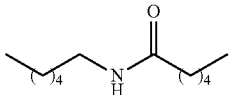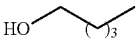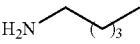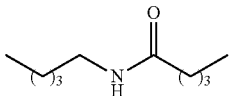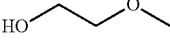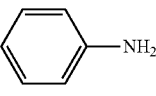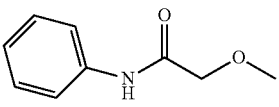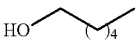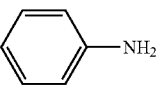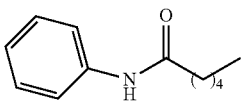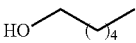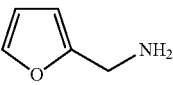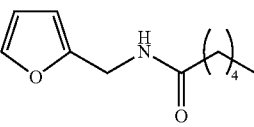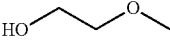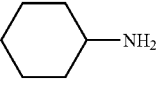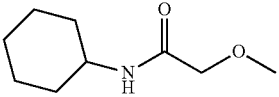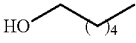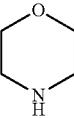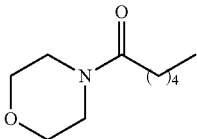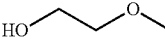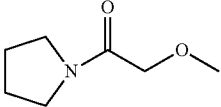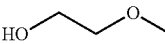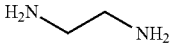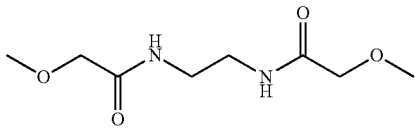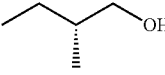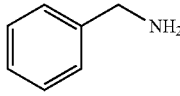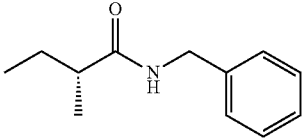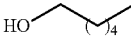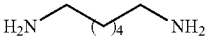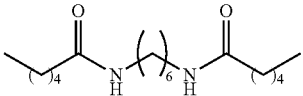
Coupling of amines and alcohols to generate amides

Entry	Alcohol	Amine	Amide	Yield (isolated)
1				95.0
2				96.3
3				97.8 (94.0)[a]
4				93.0
5				85.8
6				86.7
7				62.0
8				56.0
9				72.2
10				96.1
11				84.3

TABLE 15-continued

Coupling of amines and alcohols to generate amides

Entry	Alcohol	Amine	Amide	Yield (isolated)
12				87.0
13				90.0
14				68[b]
15				88.4

[a]Complex 3 (0.0033 mmol), an alcohol (5.0 mmol), an amine (5.0 mmol), and benzene (3 mL) were refluxed for about 38 hrs (maximum turnover number = 1500).
[b]No racemisation was observed.

B. Catalytic Dehydrogenative Bis-Acylation of Diamines with Alcohols (Table 15; Entries 13 and 15):

Complex 3 (0.01 mmol), an alcohol (10.5 mmol), a diamine (5 mmol), and benzene (5 mL) were placed in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon flow. The reaction mixture was cooled to room temperature and the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system.

C. Amidation Reaction Under Open Air (Table 16):

To an oven dried Schlenk flask cooled to room temperature under open air were added complex 4 (0.01 mmol), an alcohol (5 mmol), an amine (5 mmol) in benzene (2 mL), followed by KO^tBu (0.01 mmol) in benzene (1 mL) and the flask was equipped with a condenser and the solution was refluxed with stirring in an open system under air for 24 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with m-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Scheme 23
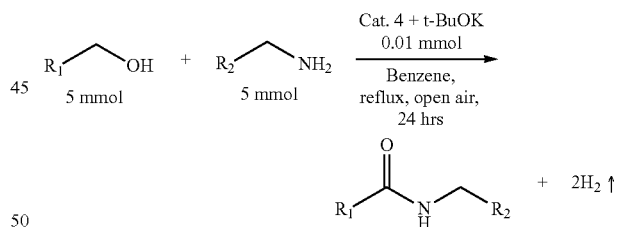
TABLE 16
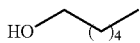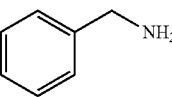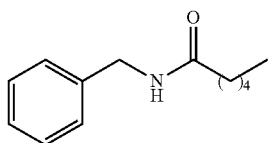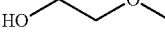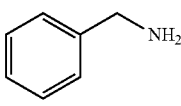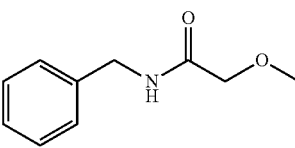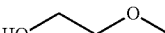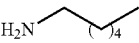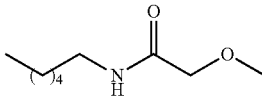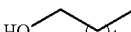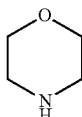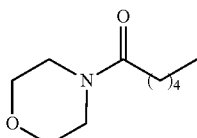
Coupling of amines and alcohols to generate amides under open air

Entry	Alcohol	Amine	Amide	Conv. of alcohol (%)	Yield (isolated)
1				77	71

TABLE 16-continued

Coupling of amines and alcohols to generate amides under open air

Entry	Alcohol	Amine	Amide	Conv. of alcohol (%)	Yield (isolated)
2				88	80
3				81	74
4				66	61

D. Amidation Reaction Under Neat Condition (Table 17):

Complex 3 (0.01 mmol), an alcohol (5 mmol), an amine (5 mmol) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was heated at 130° C. (bath temperature) with stirring in an open system under argon for 24 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with m-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Scheme 24

$$R_1 \diagdown OH \ + \ R_2 \diagdown NH_2 \ \xrightarrow[\substack{\text{Neat} \\ 130° C., Ar flow, \\ 24 hrs}]{\substack{\text{Cat. 3} \\ 0.01 mmol}} $$

5 mmol · · · · · 5 mmol

$$R_1 \diagdown \underset{O}{\overset{}{C}} \diagdown \underset{H}{N} \diagdown R_2 \ + \ 2H_2 \uparrow$$
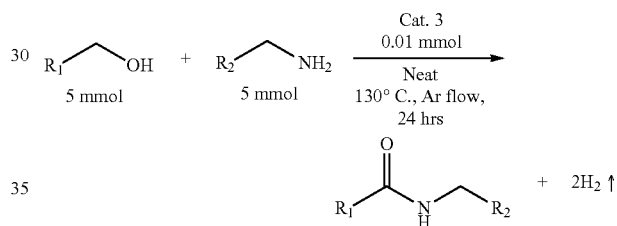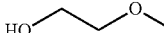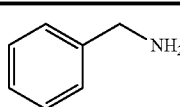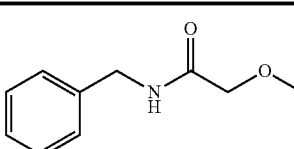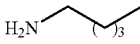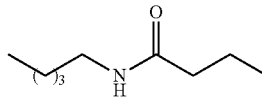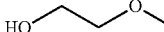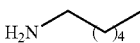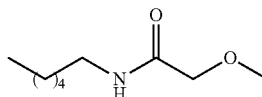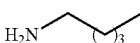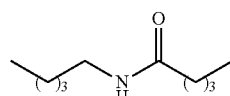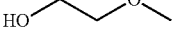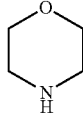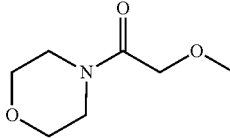
TABLE 17

Coupling of amines and alcohols to generate amides under neat conditions

Entry	Alcohol	Amine	Amide	Conv. of alcohol (%)	Yield (isolated)
1				97	87.6
2				85.2	76.0
3				92.3	82.0
4				87.0	79.6

TABLE 17-continued

				Conv. of alcohol (%)	Yield (isolated)
Entry	Alcohol	Amine	Amide		
5	HO⌒O⌒	morpholine (O,N-H ring)	morpholine-N-C(=O)-CH₂-O-CH₃	82.7	73.0

E. Amidation Reaction by In-Situ Generation of the Catalyst from the Precursor Ligand (Table 18):

To a Schlenk flask cooled under argon were added ligand, BPy-^{t}PNN (5) (0.01 mmol) and Ru-Precursor RuHCl(CO)(PPh$_3$)$_3$ (0.01 mmol), followed by benzene (1 mL) and the solution was heated (~80° C.) with stirring for about 1 hr. After cooling to room temperature, were added an alcohol (5 mmol), an amine (5 mmol), and t-BuOK (0.01 mmol) in benzene (2 mL) and the solution was refluxed with stirring in an open system under air for 24 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with m-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Purification of Amides:

After completion of the reaction, the solvent was removed (Table 15-16, and 18) under vacuum and the resulting residue was purified by the column chromatography on silica gel using EtOAc/n-hexane.

Example 5

Polyamides Synthesis from Diols and Diamines

The applicants have unexpectedly discovered that the catalysts of the present invention also catalyze the synthesis of polyamides directly from diols and diamines. In some preferred embodiments, 1,4-dioxane is used as a solvent. This polyamidation reaction is general, environmentally benign and atom economical. It proceeds under neutral reaction conditions without the use of activators, condensing agents or other additives. Moreover, these methods produce H$_2$ as the only byproduct (Scheme 26).

Scheme 25

$$R_1 \diagdown OH + R_2 \diagdown NH_2 \xrightarrow[\substack{Benzene \\ reflux,\ open\ air, \\ 24\ hrs}]{\substack{Ligand\ (BPy-^tPNN)\ 5\ + \\ HClCORu(PPh_3)_3\ + \\ KO^tBu \\ 0.01\ mmol}}$$

5 mmol   5 mmol

$$R_1 \diagdown \underset{O}{\overset{\|}{C}} \diagdown \underset{H}{N} \diagdown R_2 + 2H_2 \uparrow$$

Scheme 26

$$n\ HO \diagdown R_1 \diagdown OH\ +$$

$$n\ H_2N \diagdown R_2 \diagdown NH_2 \xrightarrow[reflux\ under\ Ar]{1\ mol\ \%\ of\ cat.}$$
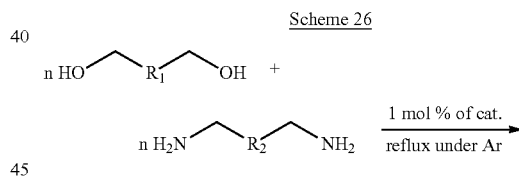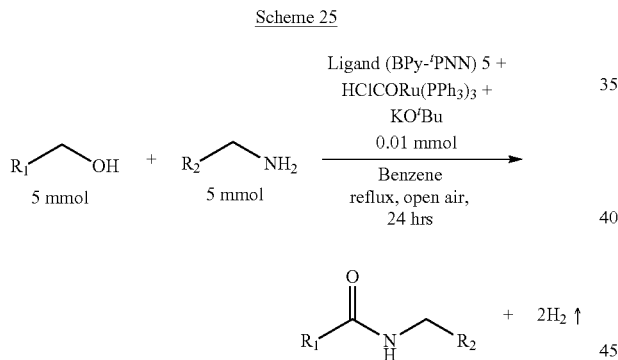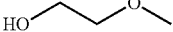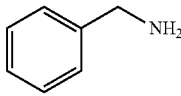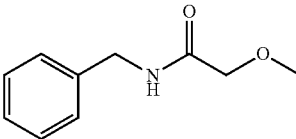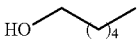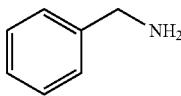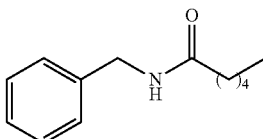
TABLE 18

Coupling of amines and alcohols to generate amides with in-situ generation of catalyst

Entry	Alcohol	Amine	Amide	Yield (isolated)
1	HO⌒O⌒	benzyl-NH₂	benzyl-NH-C(=O)-CH₂-O-CH₃	72.0
2	HO⌒(⌒)₄	benzyl-NH₂	benzyl-NH-C(=O)-(⌒)₄	67.6

-continued

Upon refluxing a 1,4-dioxane solution containing equimolar amounts of 1,6-hexanediol and 1,6-hexanediamine in the presence of 1 mol % of complex 1 under an argon atmosphere for 3 days, a white solid separated out in the reaction mixture. The solid was filtered off and successively washed with THF: EtOAc (1:1), dichloromethane and 20% methanol in water. The resultant white solid was dried under high vacuum at 80° C. for 12 hrs to afford polymer 3a in 82% yield (Table 19, entry 1). The solid was insoluble in MeOH, THF, 1,4-dioxane and chlorinated solvents, partially soluble in dimethylsulfoxide and dimethylformamide upon warming. The polyamide obtained was dissolved in deuterated trifluoroacetic acid (TFA) or trifluoroethanol (TFE) and characterized by NMR. The presence of CH_2 attached to the carbonyl group was confirmed by ^1H NMR, showing a broad singlet at 2.39 ppm for the four hydrogen atoms. A peak at 180.4 ppm in the ^{13}C $\{^1H\}$ NMR spectrum and an IR band at 1633 cm^{-1} confirm the presence of the amide C=O group. The average molecular weight M_n of the polyamide 3a was 16.6 kDa as measured by ^1H NMR using trifluoroethanol (TFE) as a solvent. The obtained solid was dissolved in TFA:CH$_3$CN (1:1) and MALDI-TOF mass spectrum was recorded using DHB (2,5-dihydroxybenzoic acid) as the matrix (FIG. 5A). The polyamide has three possible types of end groups (amine-amine, amine-alcohol or alcohol-alcohol, compounds 3aa, 3ab and 3ac, respectively) and it also might result in a cyclic form. The spectrum revealed the highest molecular weight of 4195 Da, which corresponds to a polyamide having 18 monomers with OH/OH end groups. Due to insolubility of the polymer in DMF, GPC (gel permeation chromatography) was not performed.

Different Types of End Groups in Polyamide 3a:

plexes 1 and 3 exhibit similar catalytic activity in the polyamidation reaction. However, using complex 3 it is possible to perform the polyamidation reaction in the absence of solvent, and using a lower catalyst loading. Thus, heating equivalent amounts of 1,6-hexanediol and 1,6-hexanediamine with the thermally stable complex 3 (0.2 mol %) in the absence of solvent at 130° C. for 14 hrs, followed by heating to 190° C. for an hour under Argon flow and cooling to room temperature resulted in a solid (Table 19, entry 16). The solid was washed with THF, water, ethanol and hexane and dried under vacuum for 12 hrs and isolated in 84% yield. The MALDI-TOF mass spectrum of this solid exhibited a highest molecular weight of 4951 Da. The higher molecular weight obtained under these conditions is likely due to the higher temperatures employed and absence of solvent, allowing polymerization in the melt.

Refluxing of 1,10-decanediol and 1,6-hexanediamine in 1,4-dioxane in the presence of 1 mol % of complex 1 resulted in 88% yield of the polyamide 3b (Table 19, entry 2). The presence of the amide functional group of 3b was confirmed by IR, showing an absorption frequency at 1637 cm^{-1} and a signal at 181.6 ppm in the $^{13}C\{^1H\}$ NMR spectrum. The number average molecular weight of 3b was found to be 10.3 kDa based on ^1H NMR spectra using trifluoroethanol (TFE) as a solvent. A MALDI-TOF mass spectrum indicated a molecular weight up to 4965 Da, which corresponds to a polyamide comprised of 18 monomers. Due to insolubility in DMF, GPC was not performed.

To further investigate the polyamidation reaction, various combinations of diols and diamines were studied. Thus, polyamidation reaction of 1,3-phenylenedimethanol and 1,6-hexanediamine with 1 mol % of complex 1 under argon atmosphere for 3 days resulted in a solid which was isolated by filtration. The solid was washed successively with THF: EtOAC (1:1), dichloromethane and 20% MeOH in water, and finally dried under high vacuum at 80° C. to afford 82% of compound 3c (Table 19, entry 3). The IR spectrum of the polyamide 3c showed the presence of the NH group as broad

3aa

3ab

3ac

The same reaction was performed using the bipyridine based complex 3 as catalyst. After 3 days in refluxing dioxane polymer 3a was formed as a white solid and isolated after work-up in 78% yield. Analysis of the obtained solid exhibited a similar MALDI-TOF pattern and ^1HNMR spectrum as observed with catalyst 1. Thus, under these conditions complexes

peak at 3297 cm^{-1} and the amide C=O peak at 1631 cm^{-1}. The $^{13}C\{^1H\}$ NMR spectrum exhibited the C=O carbon at 165.8 ppm. Polyamide 3c was further analyzed by MALDI-TOF by dissolving it in 80% TFA in acetonitrile using DHB as matrix (FIG. 5B). It gave a series of peaks in the range of 700-5932 Da. In an attempt to get a higher molecular weight,

polyamide 3c was refluxed with- or without 1,3-phenylene-dimethanol in the presence of the complex 1. However, a higher molecular weight was not observed. This might be due to the insolubility of 3c in 1,4-dioxane. Due to insolubility in DMF, GPC analysis was not performed.)

pyridine-2,6-diyldimethanol and 1,6-hexanediamine catalyzed by 1 mol % 1, furnished after 3 days of reflux in 1,4-dioxane the polyamide 3g (Table 19, entry 7) as a gummy insoluble solid which separated out from the reaction mixture and after work up gave a yield of 74%. The NMR and IR

3c
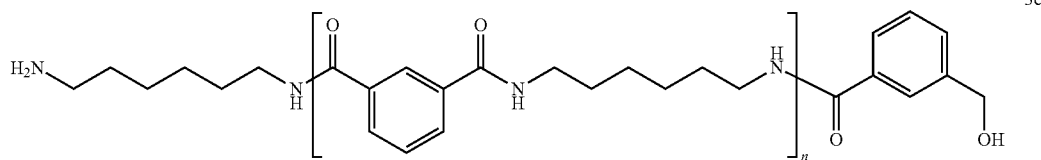
In order to increase the solubility of the polyamides, ether substituted aromatic diols were employed for the polymerization reactions. Thus, the reaction of (5-methoxy-1,3-phenylene)dimethanol and 1,6-hexanediamine gave 86% of compound 3d (Table 19, entry 4) as a gummy solid and exhibited a mass peak at 7199 Da in the MALDI-TOF spectrum using HBA+NaI as a matrix and a solution of the polyamide 3d in TFA:dichloromethane 1:1 (FIG. 5C). The polyamide 3d was dissolved completely in warm DMF and the molecular weight was measured using gel-permeation chromatography (GPC) using DMF with 0.1% LiBr (wt/v) as the eluent at a flow rate of 1.0 mL/min with column temperature at 50° C., yielding Mn=18.7 kDa with PDI of 2.08. The significantly lower molecular weight in MALDI-TOF when compared with GPC is likely to be a result of the high PDI. As previously reported, in case of polydispersities higher than PDI=1.2, MALDI-TOF leads to under-represented high-mass components with respect to the lower mass components, resulting in significantly lower average molecular weight values.

Exploring the scope of the polyamidation reaction, equivalent amounts of 1,4-phenylenedimethanol and 1,6-hexanediamine were refluxed with 1 mol % of complex 1 for 3 days, leading to 88% yield of the crude compound 3e (Table 19,

spectra confirm the presence of the amide carbonyl group. GPC analysis was performed for polyamide 3g using DMF as a solvent upon heating at 80° C. The Mn calculated from the GPC was 26.9 kDa with PDI of 1.98. The polyamide 3g was also analyzed by MALDI-TOF. The MALDI-TOF mass spectrum shows a series of peaks in the range of 600-4700 Da and the highest mass peak at 4583 appeared with low intensity and corresponds to 18 monomer units.

Next, aromatic diamines were studied for polyamidation reactions. Upon refluxing 1,4-phenylenedimethanol and 1,3-phenylenedimethanamine, a white solid was obtained after 3 days and was filtered off and dried under vacuum to provide 86% of polyamide 3h (Table 19, entry 8). The NMR and MALDI-TOF of 3h (FIG. 5E) reveal high molecular weight oligomeric mixtures. The highest mass unit obtained for the polyamide 3h was 3861 Da, having amine end groups and corresponding to 14 monomer units in the chain. The other oligomer peaks appear at 3594, 3328, 3062, 2796, 2530, 2264, 1732, 1466, 1200, 668 mass units. Further, heating the compound 3h in refluxing 1,4-dioxane in the presence of 1 mol % of the catalyst 1 did not result in progress of the polymer chain (due to insolubility in DMF, GPC analysis was not performed).

3h
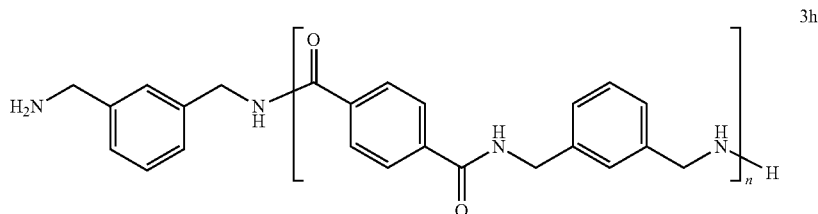
entry 6). Successive washings with THF:EtOAC (1:1), dichloromethane, and 20% MeOH in water resulted in 80% yield of the solid after drying under vacuum. IR (peak at 1626 cm^{-1}) and NMR spectra confirm the presence of amide functionality. MALDI-TOF spectrum of the compound 3e in TFA: CH$_3$CN (1:1) revealed only oligomeric mixtures in the range of 700-2500 Da (FIG. 5D). The mass unit of 2322 Da corresponds to only 9 monomer units. Reaction of the shorter diamine 1,2-ethylenediamine with 1,4-phenylenedimethanol did not result in significant progress of the polyamidation reaction, giving the polyamide 3f in 63% yield (Table 19, entry 6), comprised of low molecular weight oligomeric mixtures in the range of 600-1900.

Next, the polyamidation reaction was examined using heteroaromatic diols. Thus, reaction of equivalent amounts of

The polyamidation reaction of 1,4-phenylenedimethanol and 1,4-phenylenedimethanamine afforded a mixture of oligomers 3i in 84% isolated yield (Table 19, entry 9). The MALDI-TOF spectrum showed the highest mass unit of 3747 Da, indicating the presence of 14 monomer units. The reaction of 1,3-phenylenedimethanol and 1,3-phenylenedimethanamine led to 3j (Table 19, entry 10) in 78% yield after workup, with a maximum mass unit of 1467, corresponding to 5.5 monomer units. The reaction of 1,5-pentanediol and 1,4-phenylenedimethanamine gave 80% of compound 3k (Table 19, entry 11). Interestingly, 3k showed a series of mass peaks in the range of 500-5200 Da corresponding to 22 monomer units. Reaction of cyclohexane-1,4-diyldimethanol and 1,4-phenylenedimethanamine gave 66% of compound 3l (Table 15, entry 12), with peaks at 1912 Da corresponding to

only 7 monomeric units in MALDI-TOF spectrum. (Due to insolubility in DMF, GPC analysis was not performed.)

Polyamidation of (5-methoxy-1,3-phenylene)dimethanol, 1,4-phenylenedimethanamine using 1 mol % catalyst 1 afforded compound 3m (Table 19, entry 13) in 76% yield, with the mass obtained at 4450 Da by MALDI-TOF, corresponding to 15 monomer units. The GPC analysis of 3m showed a molecular weight Mn=5.3 kDa. Similarly, the reaction of (5-(hexyloxy)-1,3-phenylene)dimethanol and 1,3-phenylenedimethanamine gave 88% of the polyamide 3n (Table 19, entry 14). The number average molecular weight Mn of 3n was 11.3 kDa based on GPC analysis. Reaction of (5-(hexyloxy)-1,3-phenylene)dimethanol and 1,4-phenylenedimethanamine gave 77% of the polyamide 3o (Table

15, entry 15) with a mass of 3052 Da corresponding to 8 monomers based on the MALDI-TOF spectrum.

Thus, a variety of polyamides have been synthesized having different spacers in good yield. The synthesis of polyamides using non-activated/non-ether linked substrates was demonstrated. The synthesized polyamides were characterized by spectroscopic techniques. The molecular weight was determined by ^{1}H NMR and GPC analysis. The heteroaromatic polyamide 3g gave the highest number average molecular weight compared to the corresponding aliphatic and aromatic derived polyamides (3a and 3d respectively). MALDI-TOF spectra of insoluble polyamides was also obtained. The results are summarized in Table 19.

TABLE 19

Catalytic polyamidation using diols and diamines.[a]						
Entry	Diols	Diamines	Polyamides	Isolated Yield (%)	Highest molecular weight by MALDI-TOF (Da)	Mn (10³)	PDI
1				82	4195	16.6[b]	—
2				88	5000	10.3[b]	—
3				82	5932	—	—
4				86	7199	18.7[c]	2.08
5				80	2322	—	—

TABLE 19-continued
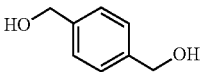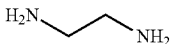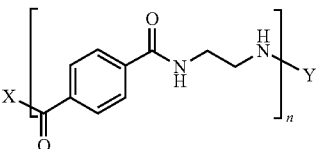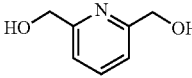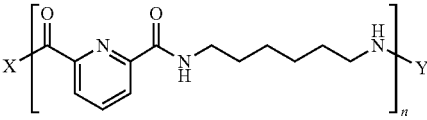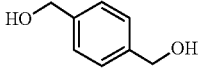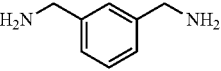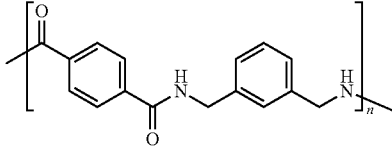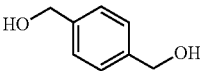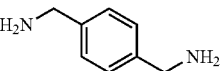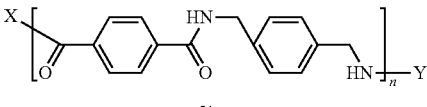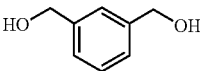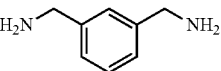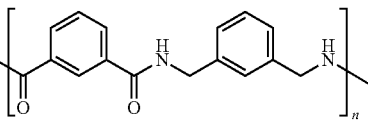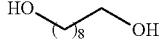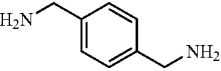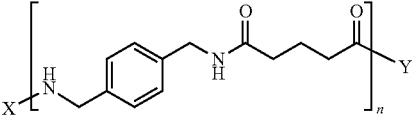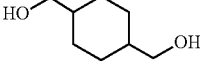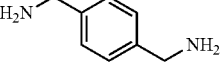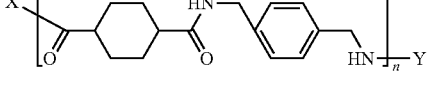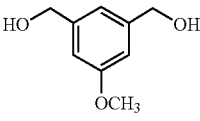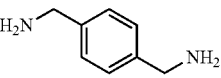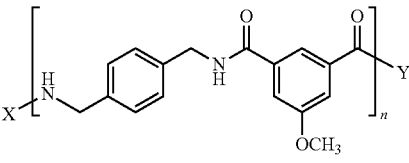
Catalytic polyamidation using diols and diamines.[a]

En-try	Diols	Diamines	Polyamides	Iso-lated Yield (%)	Highest mo-lecular weight by MALDI-TOF (Da)	Mn (10³)	PDI
6			3f	63	1849	—	—
7			3g	74	4583	26.9[c]	1.98
8			3h	86	3861	—	—
9			3i	84	3734	—	—
10			3j	78	1467	—	—
11			3k	80	5200	—	—
12			3l	66	1912	—	—
13			3m	76	4450	5.3[c]	3.20

TABLE 19-continued

Catalytic polyamidation using diols and diamines.[a]

En-try	Diols	Diamines	Polyamides	Iso-lated Yield (%)	Highest molecular weight by MALDI-TOF (Da)	Mn (10³)	PDI
14			3n	88	—	11.3[c]	2.18
15			3o	77	3052	5.4[c]	2.51
16[d]			3a	84	4951	—	—

[a]Complex 1 (0.01 mmol), diol (1 mmol), diamine (1 mmol) and 1,4-dioxane (2 mL) were refluxed at an oil bath temperature of 135° C. in a Schlenk tube under Argon for 3 days.
[b]Mn was calculated from ¹H NMR
[c]Mn was obtained from GPC analysis
[d]No solvent was used. Catalyzed by complex 3.
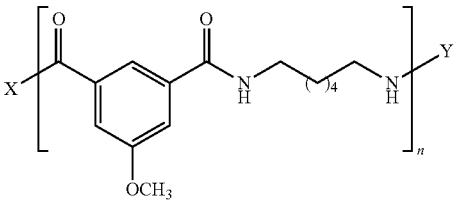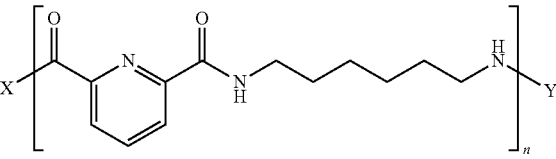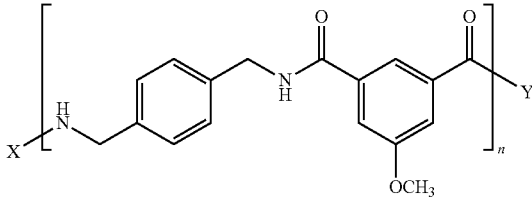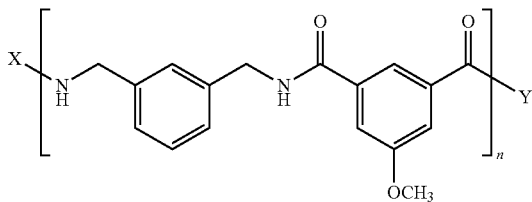
Thermogravimetric analyses (TGA) of the synthesized polyamides were performed. Weight losses of 30% and 50% occurred at similar temperatures and were not significantly dependent on polymer structure (FIG. 6, Table 20). However, the aliphatic polyamide 3a was less thermally stable and exhibited 83% weight loss at 495° C., while the arene-based polyamides 3d, m, n (except 3g) exhibited 62-70% weight loss at 680° C. (Table 20). The pyridine-based polyamide 3g was less stable, and exhibited 92% weight loss at 520° C.

TABLE 20

Thermal studies of polyamides 3 at various temperatures by TGA.

Polyamides	Mn (10³¹)	T (° C. at 5% weight loss)	T (° C. at 10% weight loss)	T (° C. at 30% weight loss)	T (° C. at 50% weight loss)	T (° C. at 70% weight loss)
3a	16.6	360	395	425	437	451 (70%) 495 (83%)

TABLE 20-continued

Thermal studies of polyamides 3 at various temperatures by TGA.

Polyamides	Mn $(10^{3\text{D}})$	T (° C. at 5% weight loss)	T (° C. at 10% weight loss)	T (° C. at 30% weight loss)	T (° C. at 50% weight loss)	T (° C. at 70% weight loss)
3d	18.7	120	170	430	458	680 (62%)
3g	26.9	100	380	458	470	478 (70%) 520 (92%)
3m	5.3	180	350	402	430	680 (64%)
3n	11.3	140	170	400	420	680 (64%)

Polymerization with Catalyst 3:

Synthesis of Nylon-6,6 by Catalytic Method Under Neat Condition:

Complex 3 (0.01 mmol), 1,6-hexanediol (5 mmol), and 1,6-hexanediamine (5 mmol) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and gradually heated up to 135° C. (bath temperature) and continued the heating at the same temperature with stirring in an open system under argon for 14 hrs. During the heating effervescence was observed and the viscous liquid became solid. After cooling to room temperature, the solid thus obtained (low molecular weight oligomer; m.p=215.9° C. (by TGA)) was again heated up to 190° C. using sand bath for about an hour in an open system under argon. The resulting solid was washed with THF, water, ethanol and finally with hexane (in order to remove other impurities) and dried under vacuum for overnight.

Scheme 27

Nylon-6,6
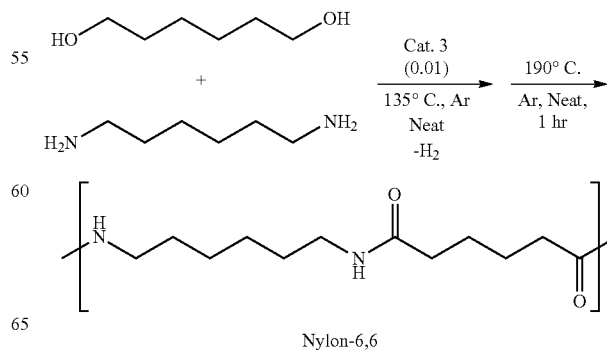
DSC:

Temperature (° C.)	Weight loss (in %)
100	2.70
200	3.5
300	5.7
350	8.47
400	22.2
450	62.2
500	64.7
550	65.5
600	66.0

TGA: m.p 251.9° C. (regenerated with the same melting point after 4 cycles with freezing point of 216.1° C.).

MOLDI-TOF: (matrix=DHB (2,5-dihydroxybenzoicacid), solvent=trifluoroethanol:CH_2Cl_2) up to 4800 Da.

In conclusion, polyamidation based on coupling of non-activated diols and diamines, with extrusion of H_2, catalyzed by complexes 1 and 3 was developed. Guan et al have also reported the utilization of the amidation reaction catalyzed by complex 1 for the preparation of other polyamides, bearing ether-functionalized spacers. The polyamidation reaction proceeds under neutral conditions, with liberation of molecular hydrogen and with no preactivation of the substrate being required. The reaction can be applied to a variety of diols and diamines for the synthesis of functional polyamides. The number average molecular weight of the polymers obtained in our work was measured by ^{1}H NMR, MALDI-TOF and, in case of the DMF-soluble polymers, by GPC analysis. Mean molecular weights up to 26.9 kDa were obtained, with polydispersities in the range of PDI=1.98-3.2. The variation in chain lengths for different substrate combinations is probably influenced by the different solubilities of the polymers. The insoluble polyamides were characterised spectroscpoically and by MALDI-TOF. It was observed that molecular weights determined by GPC were significantly higher than those obtained by MALDI-TOF. This is another example of the MALDI-TOF method favoring lower molecular weights in case of PDI>1.2 The thermal properties of the polyamides with different spacers were studied and it was found that aliphatic/pyridinic spacer-based polyamides are less stable at high temperature as compared with aromatic derived polyamides. Polyamidation in absence of solvent was also demonstrated. This simple, environmentally benign and general polymerization reaction provides a new approach to the important area of polyamide synthesis.

General Procedure for the Catalytic Direct Polyamidation of Diols with Diamines Catalyzed by Complex 1:

Complex 1 (0.01 mmol), diol (1 mmol), amine (1 mmol), and 1,4-dioxane (2 mL) were added to schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon flow for 3 days. During the course of the reaction, a white colored solid separated out for 24 hrs. The reflux was continued for 3 days. After cooling to room temperature, the solid obtained was filtered and washed successively with methanol and dichloromethane, or with THF:ethylacetate (1:1), dichloromethane and 20% methanol in water to give the product polyamide. T. The solid obtained was dried under vacuum at 80° C. for 8-12 hrs. The products were analyzed by NMR, IR and MALDI TOF.

Spectral Data for Polyamides:
Polyamide 3a:
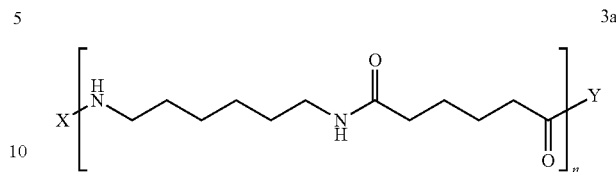
IR (KBr pellet): 3304, 2935, 2859, 1633, 1536, 1474, 1276 cm^{-1}; ^{1}H NMR (TFA-d): 1.08 (broad s, 4H), 1.34 (broad s, 4H), 1.52 (broad s, 4H), 2.39 (broad s, 4H), 3.17 (broad s, 4H); ^{13}C{^{1}H}NMR (TFA-d): 26.8, 27.8, 29.5, 35.0, 44.5, 180.4.

MALDI-TOF (matrix: HBA (2,5-dihydroxybenzoic acid), solvent acetonitrile: TFA): m/z=569 to 4195 Da. The spectrum of polyamide 3a shows a series of peaks at 569 (3aa+H$^+$ (n=2)), 795 (3aa+H$^+$ (n=3)), 909 (3ab+H$^+$(n=3)), 1022 (3c (n=4)), 1135 (3ab+H$^+$ (n=4)), 1247 (3aa+H$^+$ (n=5)), 1361 (3ab+H$^+$ (n=5)), 1474 (3ac(n=6)), 1588 (3ab+2H$^+$ (n=6)), 1700 (3ac (n=7)), 1814 (3ab+2H$^+$ (n=7)), 1926 (3ac (n=8)), 2041 (3ab+3H$^+$ (n=8)), 2153 (3ac+H$^+$ (n=9)), 2266 (3ab+2H$^+$ (n=9)), 2379 (3ac+H$^+$ (n=10)), 2494 (3ab+4H$^+$ (n=10)), 2606 (3ac+2H$^+$ (n=11)), 2720 (3ab+4H$^+$ (n=11)), 2832 (3ac+2H$^+$ (n=12)), 2947 (3ab+5H$^+$ (n=12)), 3058 (3ac+2H$^+$ (n=13)), 3170 (3ab+H$^+$ (n=13)), 3288 (3ac+6H$^+$ (n=14)), 3402 (3ab+8H$^+$ (n=14)), 3515 (3ac+7H$^+$ (n=15)), 3625, 3739 (3ac+5H$^+$ (n=16)), 3840, 3853, 3966 (3ac+5H$^+$ (n=17)), 4079 (3ab+6H$^+$ (n=13)), 4195 (3ac+9H$^+$ (n=18)).

Polyamide 3b:
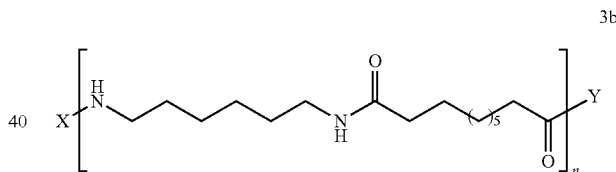
IR (KBr pellet): 3306, 2933, 2854, 1637, 1540, 1437, 1383, 1239 cm^{-1}; ^{1}H NMR (TFA-d): 1.28 (broad s, 12H), 1.63 (broad s, 8H), 2.61 (broad s, 4H), 3.46 (broad s, 4H); ^{13}C{^{1}H}NMR (TFA-d): 27.6, 29.3, 30.4, 35.5, 44.7, 181.6. MALDI-TOF (matrix: HBA (2,5-dihydroxybenzoic acid)+ NaI, solvent dichloromethane: TFA): m/z=1258 to 4965 Da.

Polyamide 3c:
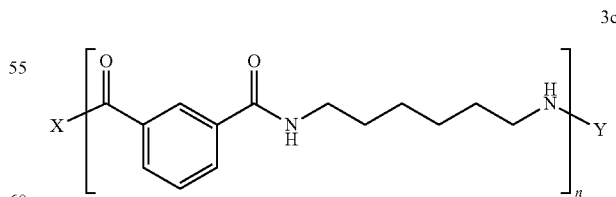
IR (KBr pellet): 3297, 2935, 2857, 1631, 1532, 1274 cm^{-1}; ^{1}H NMR (DMSO-d$_6$): 1.32 (broad s, 4H, CH_2), 1.51 (broad s, 4H, CH_2), 3.23-3.32 (m, 4H, NCH_2), 7.50 (t, 1H, =CH), 7.91 (d, 2H, =CH), 8.26 (s, 1H, =CH), 8.54 (broad s, 2H, NH). ^{13}C{^{1}H}NMR (DMSO-d$_6$): 26.2, 29.1, 39.2, 126.1, 128.2, 129.5, 134.9, 165.8. MALDI-TOF (matrix: 2,5-dihydroxy-

benzoic acid, solvent acetonitrile:TFA): m/z=700 to 5932 Da. The following peaks were observed: 5932 (3c (n=23)+24), 5918 (3c (n=23)+10), 5685 (3c (n=22)+23), 5671 (3c (n=22)+9), 5439 (3c (n=21)+23), 5425 (3c (n=21)+9), 5192 (3c (n=20)+22), 5178 (3c (n=20)+8), 4946 (3c (n=19)+22), 4932 (3c (n=19)+8), 4699 (3c (n=18)+21), 4685 (3c (n=18)+7), 4453 (3c (n=17)+21), 4439 (3c (n=17)+7), 4207 (3c (n=16)+21), 4193 (3c (n=16)+7), 3961 (3c (n=15)+21), 3947 (3c (n=15)+7), 3714 (3c (n=14)+20), 3700 (3c (n=14)+6), 3468 (3c (n=13)+20), 3454 (3c (n=13)+6), 3219 (3c (n=12)+17), 3205 (3c (n=12)+3), 2973 (3c (n=11)+17), 2959 (3c (n=11)+3), 2727 (3c (n=10)+17), 2713 (3c (n=10)+3), 2481 (3c (n=9)+17), 2467 (3c (n=9)+3), 2234 (3c (n=8)+16), 2220 (3c (n=8)+2), 1988 (3c (n=7)+16), 1974 (3c (n=7)+2), 1742 (3c (n=6)+16), 1728 (3c (n=6)+2), 1496 (3c (n=5)+16), 1482 (3c (n=5)+2). The excess mass units are due to the protonation of the amine functionality in TFA.

Polyamide 3d:
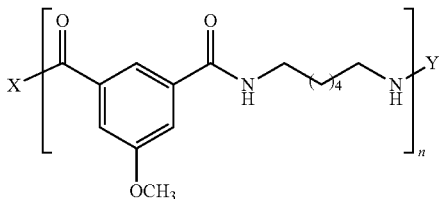
^{1}H NMR (DMSO-d_6): 1.32 (broad s, 4H, CH_2), 1.51 (broad s, 4H, CH_2), 3.15 (s, 2H, NCH_2), 3.38 (broad s, 2H, NCH_2), 3.82 (s, 3H, OCH_3), 7.48 (s, 2H, =CH), 7.88 (s, 1H, =CH), 8.53 (broad s, 2H, NH); ^{13}C{^{1}H}NMR (DMSO-d_6): 26.3, 29.1, 48.6, 55.6, 66.4, 115.0, 119.1, 136.3, 159.1, 165.6;

GPC (0.1% LiBr in DMF): Mn=18.7×10^3 g/mol, Mw=39.1×10^3 g/mol

MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid+NaI, solvent dichloromethane:TFA): m/z=1116 to 7199 Da. The MALDI-TOF exhibited a series of oligomeric peaks at 1116 (3d (n=4)+8H$^+$, NH$_2$/OH), 1386 (3d (n=5)+2H$^+$, NH$_2$/OH), 1661 (3d (n=6)+H$^+$, NH$_2$/OH), 1935 (3c (n=7)+3H$^+$, cyclic), 2210 (3d (n=8)+2H$^+$, cyclic), 2484 (3d (n=9), cyclic), 2762 (3d (n=10)+2H$^+$, cyclic), 3034, 3309, 3582, 3861, 4144 (3d (n=15), NH$_2$/OH), 4410, 4682, 4974 (3d (n=18)+2H$^+$, NH$_2$/OH), 5254 (3d (n=19)+6H$^+$, NH$_2$/OH), 5526 (3d (n=20)+2H$^+$, NH$_2$/OH), 6102 (3d (n=22)+Na+3H$^+$, NH$_2$/OH), 6351 (3d (n=23)+3, cyclic), 6641 (3d (n=24)+13, NH$_2$/OH), 6904 (3d (n=25), NH$_2$/OH) and 7199 (3d (n=26)+23, cyclic).

Polyamide 3e:
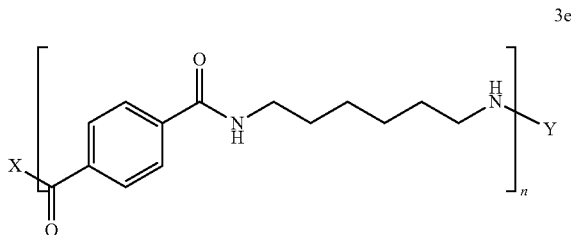
IR (KBr pellet): 3312, 2936, 2857, 1626, 1540, 1498, 1287 cm^{-1}. ^{1}H NMR (DMSO-d_6): 1.29-1.51 (m, 8H), 3.23 (broad s, 4H), 4.52 (s), 5.32 (broad s), 7.36 (d), 7.78 (d), 7.87 (s), 8.38 (t), 8.54 (broad s).

MALDI-TOF (matrix=DHB, solvent acetonitrile: TFA): m/z=743 to 2322 Da. The oligomeric peaks are 743 (3e (n=3)+H$^+$), 989 (3e (n=4)+H$^+$), 1235 (3e (n=5)+H$^+$), 1482 (3e (n=6)+2H$^+$), 1728 (3e (n=7)+H$^+$), 1973 (3e (n=8)+H$^+$), 2221 (3e (n=9)+3H$^+$), 2464 (3e (n=10)+3H$^+$).

Polyamide 3f:
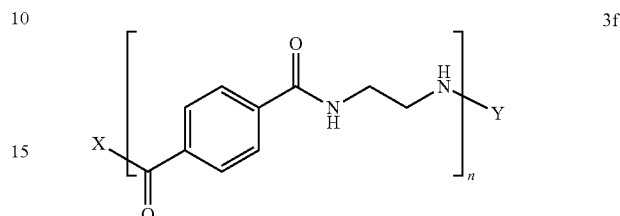
^{1}H NMR (DMSO-d_6): 2.67 (t), 3.44 (broad s), 4.53 (s), 7.37 (d), 7.80 (d), 7.90 (s), 8.56 (broad s), 8.71 (broad s). MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent: acetonitrile: TFA): m/z=765 to 1835 Da. Oligomeric peaks were observed at 765 (3f(n=4)+H$^+$), 955 (3f(n=5)+H$^+$), 1145 (3f (n=6)+H$^+$), 1335 (3f (n=7)+H$^+$), 1525 (3f (n=8)+H$^+$), 1715 (3f(n=9)+H$^+$), 1849 (3f(n=9)+H$^+$, ending with OH/OH groups).

Polyamide 3g:
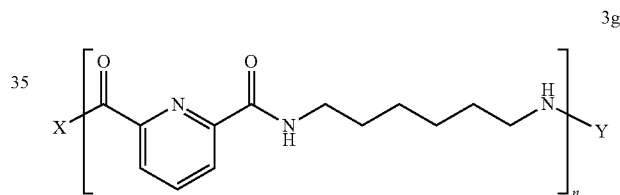
IR (KBr pellet): 3325, 2932, 2859, 1662, 1538, 1445, 1243 cm^{-1}; ^{1}H NMR (DMSO-d_6): 1.27 (broad m, 4H, CH_2), 1.50 (broad m, 4H, CH_2), 3.29 (broad s, 4H, NCH_2), 8.13 (m, 3H, =CH), 9.28 (broad s); ^{13}C NMR (DMSO-d_6): 13.9, 22.1, 26.1, 29.4, 30.9, 40.1, 124.1, 139.3, 148.8, 163;

GPC (0.1% LiBr in DMF): Mn=26.9×10^3 g/mol, Mw=53.3×10^3 g/mol

MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z=610 to 4583 Da. The spectrum exhibits a series of oligomeric peaks at 610 (3g (n=2), NH$_2$/NH$_2$), 742 (3g (n=3)+H$^+$, cyclic), 907 (3g (n=3)+Na$^+$+3H$^+$, OH/OH), 989 (3g (n=4)+H$^+$, cyclic), 1203, 1236 (3g (n=5)+H$^+$, cyclic), 1484 (3g (n=6)+2H$^+$, cyclic), 1500, 1732 (3g (n=7)+3H$^+$, cyclic), 1781, 1796, 1914, 1978 (3g (n=8)+2H$^+$, cyclic), 2063, 2079, 2092, 2210, 2226 (3g (n=9)+3H$^+$, cyclic), 2242, 2360, 2374, 2389, 2473 (3g (n=10)+3H$^+$, cyclic), 2492, 2507, 2657, 2671, 2685, 2789, 2803, 2836, 2953, 2968, 2981, 3085, 3100, 3132, 3250, 3264, 3278, 3396 (3g (n=13)+3Na$^+$, NH$_2$/NH$_2$), 3427 (3g (n=13)+KK, OK/OH), 3561, 3576 (3g (n=14)+2H$^+$, NH$_2$/NH$_2$), 3679, 3709 (3g (n=15)+3H$^+$, cyclic), 3726, 3844 (3g (n=15)+Na$^+$, NH$_2$/NH$_2$), 3975 (3g (n=16)+Na$^+$, cyclic), 4449 (3g (n=18)+3H$^+$, cyclic), 4569 (3g (n=18)+7H$^+$, NH$_2$/NH$_2$).

Polyamide 3h:

3h
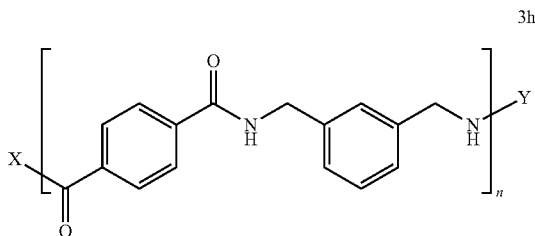
IR (KBr pellet): 3285, 2921, 1638, 1540, 1439, 1318 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): 3.68 (s), 4.47 (broad s), 7.21-7.37 (broad m), 7.92-7.94 (m), 9.15 (broad s); ^{13}C$\{^1$H$\}$NMR (DMSO-d$_6$): 42.7, 45.5, 62.6, 125.2, 125.8, 126.1, 127.2, 136.6, 139.6, 165.6; MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z=668 to 3861 Da.

Polyamide 3i:

3i
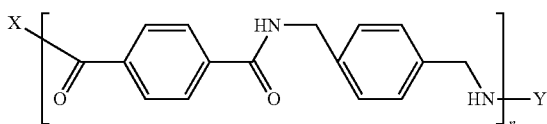
IR (KBr pellet): 3346, 3056, 2923, 1640, 1540, 1496, 1317 cm^{-1}; ^{1}H NMR (DMSO-d$_6$): 3.59 (s), 4.43 (broad m), 7.23-7.27 (broad m), 7.37 (d), 7.83 (d), 7.94 (m), 9.13 (broad s); ^{13}C$\{^1$H$\}$NMR (DMSO-d$_6$): 42.4, 45.1, 62.4, 126.0, 127.1, 132.7, 137.5, 137.9, 138.0, 138.3, 142.1, 145.9, 165.5, 166.1; MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent ACETONITRILE: TFA): m/z=400 to 3734 Da

Polyamide 3j:
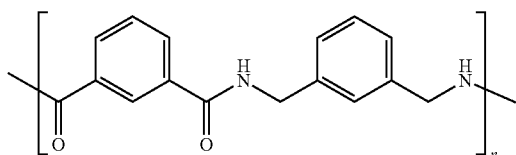
IR (KBr pellet): 3290, 3061, 2920, 1640, 1533, 1478, 1272 cm^{-1}; ^{1}H NMR (DMSO-d$_6$): 4.45-4.47 (m, 4H), 7.17-7.28 (m, 4H), 7.50 (t, 1H), 7.97 (d, 2H), 8.36 (s, 1H), 9.13 (broad m, 2H); ^{13}C$\{^1$H$\}$NMR (DMSO-d$_6$): 42.8, 66.4, 125.6, 126.5, 126.7, 128.5, 128.7, 129.9, 134.6, 139.7, 165.9.

GPC (0.1% LiBr in DMF): Mn=1.4×10^3 g/mol, Mw=5.01×10^3 g/mol

MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z=500 to 1467 Da

3k
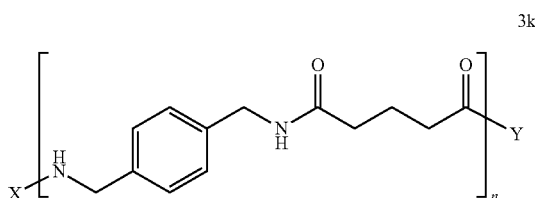
Polyamide 3k:

IR (KBr pellet): 3245, 3069, 2964, 2944, 1629, 1556, 1424, 1262 cm^{-1}; ^{1}H NMR (DMSO-d$_6$): 1.35-1.79 (m, 2H), 2.07-2.15 (m, 4H), 4.19-4.21 (broad m, 4H), 7.16 (broad s, 4H), 8.27 (broad m); ^{13}C$\{^1$H$\}$NMR (DMSO-d$_6$): 21.3, 21.9, 32.9, 35.0, 41.7, 46.8, 61.1, 127.0, 127.3, 138.1, 171.6. MALDI-TOF (matrix=DHB, solvent acetonitrile: TFA): m/z=500 to 5200 Da

Polyamide 3l:

3l
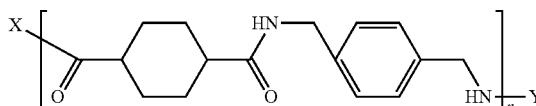
IR (KBr pellet): 3282, 3060, 2934, 2860, 1633, 1551, 1443, 1386 cm^{-1}; ^{1}H NMR (TFA-d): 7.26 (d), 7.19 (d), 7.11 (broad s), 4.44 (broad s), 4.18 (s), 3.83 (s), 2.56 (broad s), 2.00 (broad s), 0.92-1.82 (m); ^{13}C$\{^1$H$\}$NMR (TFA-d): 29.3, 45.2, 46.9, 130.6, 131.0, 131.9, 139.2, 182.7.

MALDI-TOF (matrix=DHB, solvent acetonitrile: TFA): m/z=400 to 1912 Da

Polyamide 3m:

3m
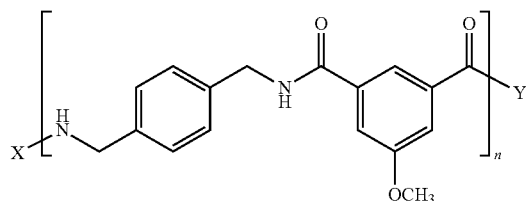
IR (KBr pellet): 3294, 3063, 2935, 1642, 1593, 1536, 1423, 1283, 1061 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): 3.56 (s), 3.81 (s), 4.42 (broad s), 7.24 (broad s), 7.54 (s), 7.96 (s), 9.11 (broad s); ^{13}C$\{^1$H$\}$NMR (DMSO-d$_6$): 42.5, 55.6, 66.3, 115.3, 118.7, 127.3, 135.9, 138.0, 159.1, 165.5, 165.8;

GPC (0.1% LiBr in DMF): Mn=5.39×10^3 g/mol, Mw=17.3737×10^3 g/mol

MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z=600 to 4450 Da

Polyamide 3n:

3n
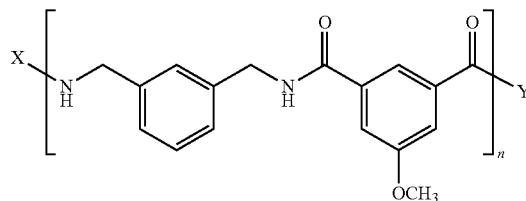
^{1}H NMR (TFA-D): 3.74 (s, 2H, NCH$_2$), 3.88 (s, 2H, NCH$_2$), 4.60 (s, 3H, OCH$_3$), 7.19-7.23 (m, 4H, Arom-H), 7.44 (s, 2H, Arom-H), 7.77 (s, 1H, Arom-H); ^{13}C$\{^1$H$\}$NMR (TFA-D): 47.2, 57.6, 68.7, 119.7, 121.1, 129.0, 129.8, 131.9, 136.3, 138.5, 162.3, 173.0; GPC (0.1% LiBr in DMF): Mn=11.3×10^3 g/mol, Mw=24.71×10^3 g/mol

Polyamide 3o:

3n
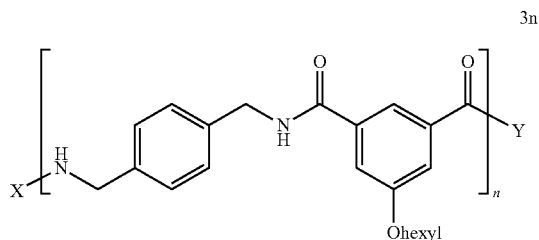
IR (KBr pellet): 3325, 3079, 2929, 2869, 1644, 1592, 1532, 1434, 1333, 1062 cm^{-1}; ^{1}H NMR (TFA-d): 7.78 (s, 1H), 7.46 (s, 2H), 7.21 (s, 4H), 4.56 (broad s, 4H), 3.94 (broad s, 2H), 1.65 (broad s, 2H), 1.26 (broad s, 2H), 1.15 (broad s, 4H), 0.70 (broad s, 3H); ^{13}C$\{^1$H$\}$NMR (TFA-d): 14.5, 24.1, 27.1, 30.5, 33.2, 47.0, 72.1, 120.4, 121.0, 130.5, 136.0, 137.8, 162.1, 173.0.

GPC (0.1% LiBr in DMF): Mn=5.4×10^3 g/mol, Mw=13.76×10^3 g/mol

MALDI-TOF (matrix=DHB, solvent acetonitrile: TFA): up to m/z=3052 Da

Example 6

Dehydrogenation of L-Alaminol to Form Poly(Alanine) Catalyzed by Ruthenium Complexes 1 or 3

Scheme 28
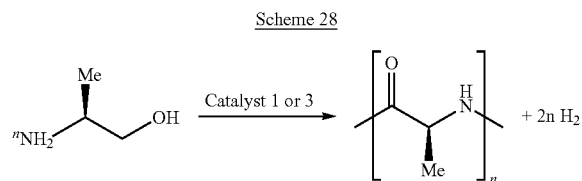
Complex 3 (0.01 mmol), L-alaninol (1 mmol), and 1,4-dioxane (2 mL) were taken in a Schlenk flask under an atmo-

sphere of purified nitrogen in a glove box. The flask was taken out the glove box, and equipped with a condenser. The solution was refluxed with stirring in an open system under argon for 48 h. After cooling to room temperature, the solvent was concentrated (~0.5 mL) under reduced vacuum followed by addition of CH$_2$Cl$_2$ (in order to remove the unreacted starting material). The white solid precipitated out from the solution at ~5° C. (after 30 min) and was collected by simple filtration and washed with toluene and dried under vacuum at 80° C. for about 14 h to yield 77% of polypeptide.

Using Complex 1 under the same procedure, 72% yield was obtained.

Poly(alanine):

mp: 190-194° C. (decompose) ^{1}H NMR (400 MHz, DMSO-d$_6$): 0.93 (broad s, 3H, CH$_3$), 4.22-4.26 (m, 1H, NCH), 8.00 (1H, CONH). ^{13}C$\{^1$H$\}$NMR (300 MHz, TFA-d$_4$): 20.0 (CH$_3$), 21.7 (CH$_3$), 53.1 (NCH), 53.4 (NCH), 174.9 (C=O).

MS (ES): 165.3 (100%, cycloala-ala+Na, $^+$), 240 (18%, M (n=1)+Na), 311 (65%, M (n=2)+Na), 382 (32%, M (n=3)+Na)), 453 (10%, M (n=4)+Na)), 524 (6%, M (n=5)+Na)).

Maldi-T of: 754 ((M (n=8)+K$^+$ H)), 903 ((M (n=10)+2Na+H)), 1001 ((M (n=12)+3H)), 1150 ((M (n=14)+10H)), 1248, 1396 ((M (n=17)+K+3H)), 1494 ((M (cyclic, n=21)+3H), 1644 ((M (n=23)+7H)). [α]=−105° (50 mg/5 mL, Acetic Acid)

Example 7

Coupling of Alcohols with water to form Acids with Liberation of H$_2$

Scheme 29
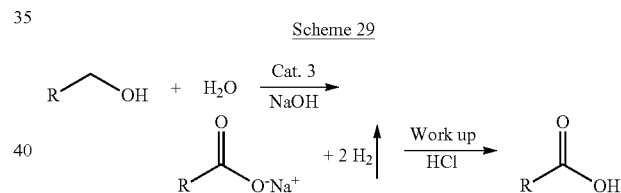
TABLE 21

Direct Transformation of Alcohols to Acids Using Water

Entry	Alcohols	Acids	Yield (%) isolated
1			84
2			88
3			78
4			73

TABLE 21-continued

Direct Transformation of Alcohols to Acids Using Water

Entry	Alcohols	Acids	Yield (%) isolated
5			78
6			80
7			74
8			63
9			91
10			89
11			83

General Procedure for the Dehydrogenation of Alcohols to Acids Catalyzed by 3:

A mixture of an alcohol (10 mmol), degassed double distilled water (2 mL) and sodium hydroxide (11 mmol) were combined in a Schlenk-flask under argon atmosphere. The biphasic mixture was degassed by purging with argon for 10 min. Complex 3 (0.02 mmol) was added and the reaction mixture was refluxed under a stream of argon. After 18 h water was added (10 mL), and the mixture was extracted with diethyl ether (2×10 mL). The aqueous phase was acidified with 5N HCl and extracted with ethyl acetate (5×20 mL). The combined extracts were washed with brine (25 mL), dried over Na_2SO_4, and evaporated under reduced pressure, affording the pure acid.

Example 8

General Experimental (Ruthenium Complex)

All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques. All solvents were reagent grade or better. All non-deuterated solvents were refluxed over sodium/benzophenone ketyl and distilled under argon atmosphere. Deuterated solvents were used as received. All solvents were degassed with argon and kept in the glove box over 4 Å molecular sieves. Most of the chemicals used in catalysis reactions were purified according to standard procedure (or by vacuum distillation/sublimation). The 6-methyl-2,2'-bipyridine (BPy-Me) and 6-chloromethyl-2,2'-bipyridine (BPy-CH$_2$Cl) precursors (Schubert et al.; Smith et al.), and RuHCl(PPh$_3$)$_3$(CO) (Ahmad et al.) were prepared according to literature procedures. Thin layer chromatography (TLC) was performed on Merck 1.05554 aluminum sheets precoated with silica gel 60 F254 and the spots visualized with UV light at 254 nm or under iodine. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60 (0.063-0.200 mm). ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at 300, 75, and 122 MHz, respectively, using Bruker AMX-300 NMR spectrometers. ^{1}H and ^{13}C{^{1}H} NMR chemical shifts are reported in ppm downfield from tetramethylsilane. ^{31}P NMR chemical shifts are reported in parts per

million downfield from H_3PO_4 and referenced to an external 85% solution of phosphoric acid in D_2O. Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were recorded on a Nicolet FT-IR spectrophotometer. Mass spectra were recorded on Micromass Platform LCZ 4000, using Electro Spray Ionization (ESI) mode. Elemental analysis were performed on Thermo Finnigan Italia S.p.A-FlashEA 1112 CHN Elemental Analyzer (manufactured by Thermo Finnigam Italia S.p.A).

Synthesis of Ligand 5:

6-methyl-2,2'-bipyridine (BPy-Me):
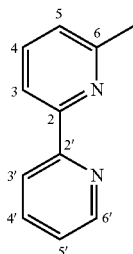
Prepared according to procedure described in *Org. Lett.* 2000, 3373 (Schubert et al.). NMR ($CDCl_3$): 2.61 (s, 3H, CH_3), 7.13 (d, 1H, J_{HH}=7.80 Hz, H-5), 7.26-7.27 (m, 1H, H-5'), 7.57 (t, 1H, J_{HH}=7.80 Hz, H-4), 7.74-7.79 (m, 1H, H-4'), 8.17 (d, 1H, J_{HH}=7.50 Hz, H-3), 8.40 (d, 1H, J_{HH}=8.10 Hz, H-3'), 8.64-8.67 (m, 1H, H-6').

6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl):
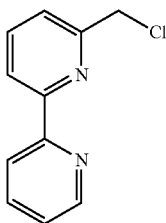
Prepared according to procedure described in *Org. Synth.* 2002, 78, 82 (Smith et al.). ^1H NMR ($CDCl_3$): 4.75 (s, 2H, CH_2), 7.27-7.32 (m, 1H), 7.49 (d, 1H, J_{HH}=7.50 Hz), 7.77-7.86 (m, 2H), 8.33 (d, 1H, J_{HH}=7.80 Hz), 8.43 (d, 1H, J_{HH}=8.10 Hz), 8.66-8.68 (m, 1H).

6-di-tert-butylphosphinomethyl-2,2'-bipyridine (BPy-^tPNN) 5:
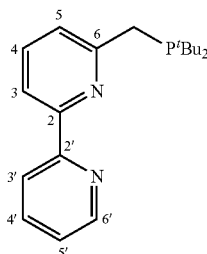
To an oven dried 50 mL pressure vessel equipped with magnetic stirring bar was added 6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl) (2.05 g, 10.00 mmol), di-tert-butyl phos-

phine (1.75 g, 12.00 mmol), and 30 mL MeOH in a nitrogen glove box. The flask was sealed and heated at 50° C. for 48 hrs with stirring outside the glove box. After cooling, it was reintroduced to the glove box, triethylamine (1.82 g, 18.00 mmol) was added and the reaction mixture was stirred at room temperature for 1 hr. The solvents were removed under reduced pressure to obtain a white solid. The residue was washed with ether (3×20 mL) and the ether filtered and was removed under reduced pressure to yield a white solid. It was recrystallized from MeOH at ca. −30° C. to yield 2.67 g (85%) of 6-di-tert-butylphosphinomethyl-2,2'-bipyridine (BPy-^tPNN).

Alternative method for the Preparation of BPy-^tPNN (5):

An oven-dried 500 mL three-necked round bottom flask equipped with an argon inlet, a stirring bar, dropping funnel and one rubber septum was cooled under a stream of argon. The flask was then charged with 6-methyl-2,2'-bipyridine (3.40 g, 20 mmol) in 80 mL dry ether. The solution was cooled to 0° C. and 13.4 mL of a 1.8 M solution of commercial lithium diisopropylamide (LDA) in heptane/THF/ethylbenzene (24 mmol) was added dropwise via syringe during 15 minutes. The resulting brown colored mixture was stirred for 1 hr at 0° C. and then cooled to −78° C. and a solution of di-tert-butylchlorophosphine (4.34 g, 24 mmol) in 30 mL dry ether was added dropwise (~30 min) to it. The stirring was continued for a further 1 hr at −78° C. and the mixture was allowed to slowly warm up to room temperature and stirred overnight. To this reaction mixture was added 40 mL of degassed water and the ether phase was separated under N_2 atmosphere. The aqueous phase was extracted with ether (2×50 mL). The combined ether solutions were dried over anhydrous Na_2SO_4, filtered under N_2 pressure, and the solvent was removed under vacuum to get brownish-white solid. This was purified by column chromatography in the nitrogen glove box (basic alumina; hexane:ether (10:1) as eluent) to yield 4.46 g (71%) of 6-di-tert-butylphosphinomethyl-2,2'-bipyridine (BPy-^tPNN) as a white solid.

$^{31}P\{^1\}$NMR (CD_2Cl_2): 37.57 (s). ^1H NMR (CD_2Cl_2): 1.17 (d, J_{PH}=11.0 Hz, 18H, P(C($CH_3)_3)_2$), 3.12 (d, J_{PH}=3.3 Hz, 2H, P—CH_2), 7.24 (ddd, J_{HH}=7.5 Hz, J_{HH}=4.8H, J_{PH}=1.2 Hz, 1H, H-5'), 7.40 (td, J_{HH}=7.8 Hz, J_{PH}=1.0H, 1H, H-5), 7.67 (t, J_{HH}=7.8 Hz, 1H, H-4), 7.76 (dt, J_{HH}=7.8 Hz, J_{HH}=1.8H, 1H, H-4'), 8.14 (br d, J_{HH}=7.8 Hz, 1H, H-3), 8.40 (td, J_{HH}=8.0 Hz, J_{HH}=1.0 Hz, 1H, H-3'), 8.62-8.64 (m, 1H, H-6'). $^{13}C\{^1H\}$NMR ($CDCl_3$): 29.61 (s, P(C($C_aH_3)_3$), 29.74 (s, P(C($C_bH_3)_3$), 31.77 (d, J_{PC}=24.0 Hz, PCH_2), 31.93 (d, J_{PC}=21.8, P(C($CH_3)_3)_2$), 117.72 (s, C-3), 121.04 (s, C-3'), 123.38 (s, C-5'), 123.85 (d, J_{PC}=8.4 Hz, C-5), 136.75, (s, C-4'), 136.91 (s, C-4), 148.98 (s, C-6'), 154.97 (s, C-2), 156.49 (s, C-2'), 161.43 (d, J_{PC}=13.8, C-6). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC. Anal. Calcd. for $C_{19}H_{27}N_2P$: C, 72.58; H, 8.66. Found: C, 72.75; H, 8.83.

Synthesis of Complexes 4 and 3:

-continued

4

$$\xrightarrow[\text{THF, -32° C.}]{\text{KO}^t\text{Bu}}$$
-KCl, -^{t}BuOH

3
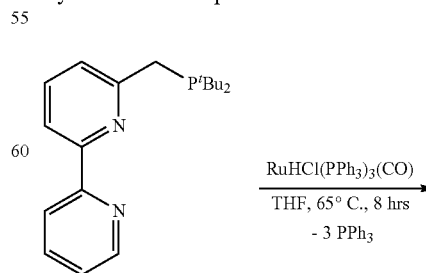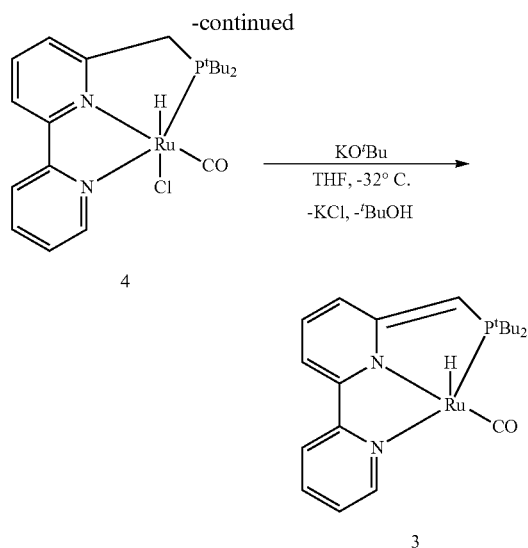
Synthesis of RuHCl(CO)(BPy-^{t}PNN) 4:

To an oven dried 25 mL pressure vessel equipped with magnetic stirring bar was added ligand, BPy-^{t}PNN (5) (157 mg, 0.52 mmol), RuHCl(CO)(PPh$_3$)$_3$ (476 mg, 0.5 mmol), and 12 mL dry THF in a nitrogen glove box. The flask was sealed and heated at 65° C. for 8 hrs with stirring outside the glove box, then cooled to room temperature to lead to reddish-brown solid. It was reintroduced to the glove box, and the solvent was decanted and the solid thus obtained was washed with ether (3×3 mL), then dried under vacuum to give pure complex 4 (212 mg, 88%).

^{31}P {^{1}H}NMR (CD$_2$Cl$_2$): 107.01 (s). ^{1}H NMR (CD$_2$Cl$_2$): −15.26 (d, ^{2}J$_{PH}$=24.6 Hz, 1H, Ru—H), 1.27 (d, J$_{PH}$=13.2 Hz, 9H, P(C(CH$_{a3}$)$_3$), 1.49 (d, J$_{PH}$=13.8 Hz, 9H, P(C(CH$_{b3}$)$_3$), AB system centered at 3.06 and 3.75 (ABq, J$_{HH}$=16.8 Hz and J$_{PH}$=10.2 Hz, 2H, PCH$_a$H$_h$), 7.44-7.46 (m, 1H, H-5'), 7.57 (d, J$_{HH}$=7.8 Hz, 1H, H-5), 7.83-7.90 (m, 2H, H-4 and H-4'), 7.97 (d, J$_{HH}$=8.1 Hz, 1H, H-3), 8.05 (d, J$_{HH}$=7.8 Hz, 1H, H-3'), 9.12-9.15 (br m, 1H, H-6'). ^{13}C {^{1}H}NMR (CD$_2$Cl$_2$): 28.63 (d, J$_{PC}$=3.8 Hz, P(C(C$_a$H$_3$)$_3$), 29.79 (d, J$_{PC}$=4.5 Hz, P(C (C$_b$H$_3$)$_3$), 36.20 (d, J$_{PC}$=24.0 Hz, PGH$_2$), 37.21 (d, J$_{PC}$=15.0 Hz, P(C$_a$(CH$_3$)$_3$), 37.27 (d, J$_{PC}$=15.8 Hz, P(C$_h$(CH$_3$)$_3$), 119.39 (s, C-3), 121.31 (s, C-3'), 122.82 (d, J$_{PC}$=9.0 Hz, C-5), 126.11 (s, C-5'), 136.30, (s, C-4'), 137.26 (s, C-4), 153.19 (s, C-6'), 154.80 (s, C-2), 155.89 (s, C-2'), 161.72 (br d, J$_{PH}$=14 Hz, C-6), 207.37 (d, J$_{PC}$=15.0 Hz, Ru—CO). IR (KBr, pellet): 1990 (vRu—H), 1906 (vCO) cm^{-1}. Anal. Calcd. for C$_{20}$H$_{28}$N$_2$OPClRu: C, 50.05; H, 5.88. Found: C, 50.28; H, 6.01. MS (ESI, MeOH): 446 (100%, (M-Cl)$^+$). The crystal suitable for a single-crystal X-ray diffraction was obtained from CD$_2$Cl$_2$ (20 mg in 0.3 mL) at −32° C. after several days.

X-Ray Crystal Structure Determination of 4:

A crystal was mounted in a MiTeGen loop and flash frozen in a nitrogen stream at 120K. Data were collected on a Nonius Kappa CCD diffractometer mounted on a FR590 generator equipped with a sealed tube with MoKa radiation (λ=0.71073 Å) and a graphite monochromator. The structure was solved using direct methods with SHELXS-97 based on F^2.

Complex 4:

C$_{20}$H$_{28}$N$_2$OPClRu, Orange, prism, 0.16×0.16×0.12 mm^3, monoclinic, P2$_1$/c, a=8.1380 (2) Å, h=14.3161 (2) Å, c=17.5802 (3) Å, β=92.253 (1) deg., V=2046.59 (7) Å^3, Z=4, fw=479.93, D$_c$=1.558 Mg/m^3, μ=0.986 mm^{-1}. Full matrix least-squares of refinement based on F^2 gave an agreement factor R=0.0326 for data with I>2σ(I) and R=0.0435 for all data (4691 reflections) with a goodness-of-fit of 0.994. Idealized hydrogen atoms were placed and refined in the riding mode, with the exception of the hydride ligand H1-Ru, which was located in the difference map and refined independently.

Synthesis of [RuH(CO)(BPy-^{t}PNN*)] 3.

3
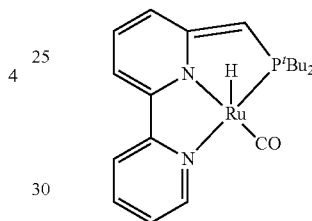
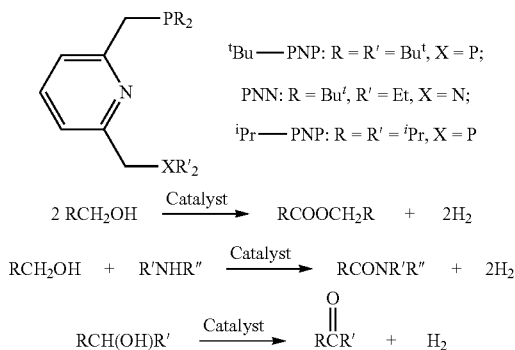(a) To a suspension of complex 4 (48 mg, 0.1 mmol) in dry THF (5 ml) in a nitrogen glove box was added KO^{t}Bu (11.2 mg, 0.1 mmol) at ca.−32° C. and the mixture was stirred at −32° C. for 3 hrs and the solvent was removed under vacuum. The product was extracted using a benzene:pentane (3:7) mixture (3×5 mL) and passed through celite. The resulting solution was concentrated under vacuum to ca. 0.5 mL and 5 mL pentane was added to cause precipitation of a greenish-block solid, which was filtered and washed with pentane (3×2 mL), then dried under vacuum (42 mg, 94%).

(b) 9.6 mg. of RuHCl(CO)(BPy^2-^{t}PNN) 4 (0.02 mmol) were placed in to a J. Young NMR tube, dissolved in ~0.4 mL of C$_6$D$_6$ and 1 eq. of potassium bis(trimethylsilyl)amide (KH-MDS, 4.0 mg) was added to generate dark-green/black complex 3. The resulting complex 3 exhibits a broad singlet at 92.70 in ^{31}P{^{1}H}NMR, and the hydride ligand appears as broad doublet at −25.73 ppm (^{2}J$_{PH}$=23 Hz) in the ^{1}HNMR spectrum.

^{31}P{^{1}H}NMR (THF-d; 202 MHz): 95.64 (s). ^{1}H NMR (THF-d; 500 MHz): −20.93 (d, ^{2}J$_{PH}$=25.0 Hz, 1H, Ru—H), 1.25 (d, J$_{PH}$=13.0 Hz, 9H, P(C(CH$_{a3}$)$_3$), 1.28 (d, J$_{PH}$ 12.5 Hz, 9H, P(C(CH$_{b3}$)$_3$), 3.36 (s, 1H, =CHP), 6.00 (d, 1H, H-3), 6.12 (d, J$_{HH}$=9.0 Hz, 1H, H-5), 6.37 (d, J$_{HH}$=8.0 Hz, 1H, H-4), 7.19 (t, J$_{HH}$=6.0 Hz, 1H, H-5'), 7.65-7.71 (m, 2H, H-3' and H-4'), 8.89-8.90 (br m, 1H, H-6'). ^{13}C{^{1}H}NMR (THF-d; 125 MHz): 30.09 (d, J$_{PC}$=5.0 Hz, P(C(C$_a$H$_3$)$_3$), 30.19 (d, J$_{PC}$=3.8 Hz, P(C(C$_b$H$_3$)$_3$), 36.20 (d, J$_{PC}$=22.5 Hz, P(C$_a$ (CH$_3$)$_3$), 37.45 (d, J$_{PC}$=27.5 Hz, P(C$_b$(CH$_3$)$_3$), 66.56 (d, J$_{PC}$=48.8 Hz, =CHP), 99.87 (s, C-3), 117.64 (d, J$_{PC}$=17.5 Hz, C-5), 121.47 (s, C-3'), 124.60, (s, C-5'), 131.81 (s, C-4), 136.92 (s, C-4'), 153.21 (s, C-6'), 155.06 (s, C-2), 161.55 (s, C-2'), 168.97 (d, J$_{PC}$=16.3 Hz, C-6), 208.1 (d, J$_{PC}$=13.8 Hz, Ru—CO). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC. IR (KBr, pellet): 2017 (vRu—H),

1907 (vCO) cm^{-1}. Anal. Calcd. for $C_{20}H_{27}N_2OPRu$: C, 54.17; H, 6.14. Found: C, 54.32; H, 6.37. MS (ESI, CH_3CN): 445 (100%, (M+1)$^+$).

Synthesis of 6-di-iso-propylphosphinomethyl-2,2'-bipyridine (BPy-^{iso}(Pr)PNN) 6:

To an oven dried 50 mL pressure vessel equipped with magnetic

6
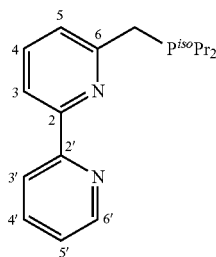
stirring bar was added 6-chloromethyl-2,2'-bipyridine (BPy-CH$_2$Cl) (1.03 g, 5.00 mmol), di-iso-propyl phosphine (710 mg, 6.00 mmol), and 15 mL MeOH in nitrogen glove box. The flask was sealed and heated at 50° C. for 48 hrs with stirring outside the glove box. After cooling, it was reintroduced to the glove box, triethylamine (910 mg, 9.00 mmol) was added and the reaction mixture was stirred at room temperature for 1 hr. The solvents were removed under reduced pressure to obtain a white solid. The residue was washed with ether (2×10 mL), filtered and was removed under reduced pressure to yield a pale yellow liquid. It was further purified by basic alumina chromatography under the glove box using hexane as an eluent to yield pure 6.

Yield=874 mg (61%). $^{31}P\{^1H\}$NMR (CD$_2$Cl$_2$): 15.84 (s). ^{1}H NMR (CD$_2$Cl$_2$): 1.11 (dd, J$_{PH}$=13.8 Hz, J$_{HH}$=7.2 Hz, 6H, P(CH(CH)$_2$), 1.17 (dd, J$_{PH}$=14.4 Hz, J$_{HH}$=7.2 Hz, 6H, P(CH (CH$_{b3}$)$_2$), 1.89 (sep d, J$_{HH}$=7.2 Hz, J$_{PH}$=2.1 Hz, 2H, P(CH (CH$_{a/b3}$)$_2$), 3.12 (d, J$_{PH}$=1.8 Hz, 2H, P—CH$_2$), 7.28-7.34 (m, 1H, H-5'), 7.33 (d merged with m, 1H, J$_{HH}$=7.8 Hz, H-5), 7.73 (t, J$_{HH}$=7.8 Hz, 1H, H-4), 7.82 (dt, J$_{HH}$=7.8 Hz, J$_{HH}$=1.8H, 1H, H-4'), 8.21 (d, J$_{HH}$=7.8 Hz, 1H, H-3), 8.46 (br d, J$_{HH}$=8.1 Hz, 1H, H-3'), 8.67-8.69 (m, 1H, H-6'). $^{13}C\{^1H\}$NMR (CD$_2$Cl$_2$): 18.89 (d, J$_{PC}$=10.5 Hz, P(C(C$_a$H$_3$)$_2$), 19.62 (d, J$_{PC}$=15.0 Hz, P(C(C$_b$H$_3$)$_2$), 23.62 (d, J$_{PC}$=15.0 Hz, PCH$_2$), 32.45 (d, J$_{PC}$=22.5, P(C(C$_{a/b}$H$_3$)$_2$), 117.63 (s, C-3), 120.77 (s, C-3'), 123.50 (s, C-5'), 123.60 (s, C-5), 136.68, (s, C-4'), 136.90 (s, C-4), 149.06 (s, C-6'), 155.18 (s. C-2), 156.38 (s, C-2'), 161.34 (d, J$_{PC}$=9.0, C-6). Assignment of signals was confirmed by DEPT 135. Anal. Calcd. for C$_{17}$H$_{23}$N$_2$P: C, 71.30; H, 8.10. Found: C, 71.52; H, 8.34.

Synthesis of RuHCl(CO)(BPy-^{iso}(Pr)PNN) 7:

7
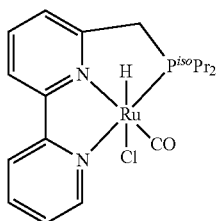
To a suspension of RuHCl(CO)(PPh$_3$)$_3$ (476 mg, 0.5 mmol) in dry THF (12 ml) in a nitrogen glove box was added

ligand, BPy-^{iso}(Pr)PNN (6) (143 mg, 0.5 mmol), and the mixture was stirred for overnight at room temperature to obtain reddish-brown solid. The solvent was decanted and the solid thus obtained was washed with pentane (3×5 mL), then dried under vacuum to give pure complex 7 (206 mg, 91%). $^{31}P\{^1H\}$ NMR (see below) of complex shows a singlet at 95.38 ppm. The ^{1}H NMR spectrum of the complex exhibits a doublet resonance at −15.26 ppm (^{2}J$_{PH}$=24.6 Hz) for Ru—H. The "arm" methylene protons give rise ABq system centered at 3.65 and 3.77 ppm with J$_{HH}$=17.4 Hz and J$_{PH}$=10.2 Hz. The BPy-C6'H appears as multiplet at 9.18-9.26 ppm, representing an upfield shift of ca. 0.53 ppm relative to the corresponding proton of the ligand (8.67-8.69 ppm), upon complexation with ruthenium.

$^{31}P\{^1H\}$NMR (CD$_2$Cl$_2$): 95.38 (s). ^{1}H NMR (CD$_2$Cl$_2$): −14.75 (d, J$_{PH}$=23.7 Hz, 1H, Ru—H), 0.95 (dd, J$_{PH}$=15.3 Hz, J$_{HH}$=6.9 Hz, 3H, P(CH(CH)$_2$), 1.12 (dd, J$_{PH}$=17.1 Hz, J$_{HH}$=6.9 Hz, 3H, P(CH(CH$_{a3}$)$_2$), 1.38 (dd, J$_{PH}$=13.2 Hz, J$_{HH}$=7.2 Hz, 3H, P(CH(CH$_{b3}$)$_2$), 1.49 (dd, J$_{PH}$=16.8 Hz, J$_{HH}$=7.2 Hz, 3H, P(CH(CH$_{b'3}$)$_2$), 2.16-2.33 (m, 1H, P(CH (CH$_{a,a'3}$)$_2$), 2.66-2.82 (m, 1H, P(CH(CH$_{b,b'3}$)$_2$), AB system centered at 3.65 and 3.77 (ABq, J$_{HH}$=17.4 Hz and J$_{PH}$=10.2 Hz, 2H, PCH$_a$H$_b$), 7.44-7.48 (m, 1H, H-5'), 7.53 (d, J$_{HH}$=7.8 Hz, 1H, H-5), 7.83-7.94 (m, 2H, H-4 and H-4'), 7.97 (d merged with m, J$_{HH}$=8.1 Hz, 1H, H-3), 8.06 (d, J$_{HH}$=8.1 Hz, 1H, H-3'), 9.18-9.26 (br m, 1H, H-6'). $^{13}C\{^1H\}$NMR (CD$_2$Cl$_2$): 17.35 (d, J$_{PC}$=4.5 Hz, P(C(C$_a$H$_3$)$_2$), 18.21 (s, P(C (C$_{a'}$H$_3$)$_2$), 19.24 (d, J$_{PC}$=5.3 Hz, P(C(C$_b$H$_3$)$_2$), 20.15 (d, J$_{PC}$=4.5 Hz, P(C(C$_{b'}$H$_3$)$_2$), 24.58 (d, J$_{PC}$=29.3 Hz, P(C$_a$ (CH$_3$)$_2$), 28.12 (d, J$_{PC}$=24.0 Hz, P(C$_b$(CH$_3$)$_2$), 40.94 (d, J$_{PC}$=21.8 Hz, PGH$_2$), 119.63 (s, C-3), 122.59 (s, C-3'), 122.80 (d, J$_{PC}$=9.8 Hz, C-5), 126.00 (s, C-5'), 136.25, (s, C-4'), 137.02 (s, C-4), 153.06 (s, C-6'), 154.47 (s, C-2), 155.99 (s, C-2'), 161.11 (d, J$_{PC}$=4.5, C-6). 207.31 (d, J$_{PC}$=15.0 Hz, Ru—CO). IR (KBr, pellet): 1962 (vRu—H), 1915 (vCO) cm^{-1}. Anal. Calcd. for C$_{18}$H$_{24}$N$_2$OPClRu: C, 47.84; H, 5.35. Found: C, 48.01; H, 5.54.

Synthesis of 6-(N,N-diethyl)aminomethyl-2,2'-bipyridine (BPy-NNN) 8:

8
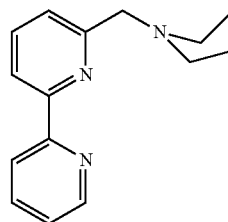
A solution of 6-chloromethyl-2,2'-bipyridine (BPy-CH$_2$Cl) in 20 mL of dry THF was cooled to 0° C. and a solution diethylamine (5 mL) in THF (10 mL) was added to it dropwise over 10 min. The mixture was allowed to slowly warm up to room temperature and refluxed under N$_2$ for 6 hrs. The solvent was removed under vacuum and the residue was dissolved in 50 mL of diethyl ether and washed with 2×10 mL of a 10% aqueous KOH solution. The organic phase was separated and dried over Na$_2$SO$_4$ and the ether was removed under vacuum. The residue was purified by flash chromatography (silica gel; EtOAc:Hexane as eluent), yielding (78% yield) 6-(N,N-diethyl)aminomethyl-2,2'-bipyridine (BPy-NNN) 8 as a yellow-brown oil.

^{1}H NMR (CDCl$_3$): 1.15 (t, J$_{HH}$=7.2 Hz, 6H, N(CH$_2$CH$_3$)$_2$), 2.70 (q, J$_{HH}$=7.2 Hz, 4H, N(CH$_2$CH$_3$)$_2$), 7.28-7.32 (m, 1H,

H-5'), 7.54 (d, J_{HH}=7.8 Hz, 1H, H-5), 7.77-7.84 (m, 2H, H-4 and H-4'), 8.26 (d, J_{HH}=8.1 Hz, 1H, H-3), 8.41 (br d, J_{HH}=8.1 Hz, 1H, H-3'), 8.67-8.69 (m, 1H, H-6'). $^{13}C\{^1H\}$NMR (CDCl$_3$): 11.69 (s, N(CH$_2$CH$_3$)$_2$), 47.36 (s, N(CH$_2$CH$_3$)$_2$), 58.81 (s, Arm-CH$_2$), 119.33 (s, C-3), 121.17 (s, C-3'), 123.26 (s, C-5'), 123.58 (s, C-5), 136.87, (s, C-4'), 137.33 (s, C-4), 149.14 (s, C-6'), 155.34 (s, C-2), 156.33 (s, C-2'), 158.68 (br s, C-6). Assignment of signals was confirmed by DEPT 135. Anal. Calcd. for C$_{15}$H$_{19}$N$_3$: C, 74.65; H, 7.94. Found: C, 74.81; H, 8.08.

Example 9

Borohydride Complexes

As contemplated herein, certain reactions described herein, such as novel ester synthesis, novel amide synthesis, as well as the dehydrogenation of secondary alcohols to ketones, and hydrogenation of esters to alcohols, can be effectively accomplished also with stable, readily synthesized PNN- and PNP Ru borohydride complexes, in absence of base, under neutral conditions, and in absence of hydrogen acceptor.

Scheme 30

^{t}Bu — PNP: R = R' = Bu^t, X = P;

PNN: R = Bu^t, R' = Et, X = N;

^{i}Pr — PNP: R = R' = ^{i}Pr, X = P

$$2\ RCH_2OH \xrightarrow{\text{Catalyst}} RCOOCH_2R + 2H_2$$

$$RCH_2OH + R'NHR'' \xrightarrow{\text{Catalyst}} RCONR'R'' + 2H_2$$

$$RCH(OH)R' \xrightarrow{\text{Catalyst}} RCR' + H_2$$

R, R', R'' can be alkyl, aryl, H)

Synthesis and Characterization of [RuH(η^2-BH$_4$)(^{t}Bu-PNP] 2'

The N$_2$-bridged binuclear Ru(II) complex [(^{t}Bu-PNP) RuCl$_2$]$_2$(μ-N$_2$) 1' was prepared by the reaction of RuCl$_2$ (PPh$_3$)$_3$ with one equivalent of ^{t}Bu-PNP (Zhang et al. 2004). Treatment of with an excess (5 equiv) of NaBH$_4$ in 2-propanol for 12 hrs resulted in formation of the Ru(II) hydrido borohydride complex 2' in almost quantitative yield (by NMR) (Scheme 25). The $^{31}P\{^1H\}$ NMR spectrum of 2' exhibits a singlet peak at 86.3 ppm, representing a downfield shift of 21 ppm relative to 1' (65.0 ppm). In the NMR spectrum, the hydride ligand gives rise to a triplet peak at –16.09 ppm with J_{PH}=18.0 Hz. In addition, two broad signals are observed for the two bridging hydrides at –16.01 and –4.48 ppm and another broad feature at 5.49 ppm belonging to the terminal boron hydrides. The IR spectrum of 2' indicates two strong bands in the terminal B—H region at 2395 and 2327 cm^{-1} and two bands in the bridging M–H—B region at 2104 and 2024 cm,$^{-1}$ consistent with the bidentate η^2-BH$_4$ binding mode (Marks et al.).

Scheme 31

$$4\ NaBH_4 \xrightarrow[\text{– 4NaCl, –2BH}_3]{\text{r.t., 12 h}}$$

2'

(P = P^{t}Bu$_2$)
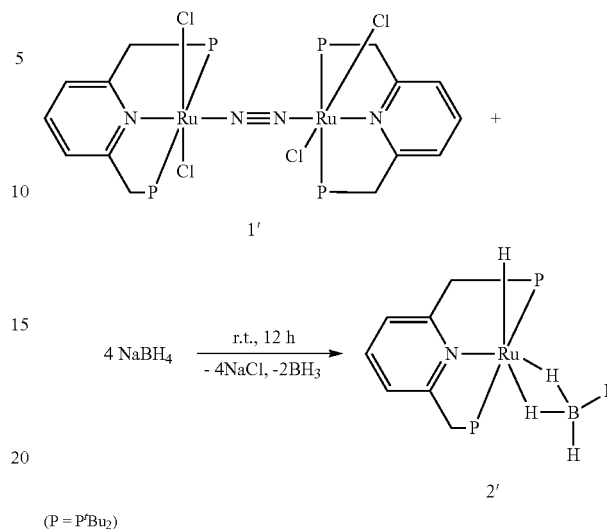
Single crystals suitable for an X-ray diffraction study were obtained by slow evaporation of a pentane solution of 2' at –32'° C. The crystal structure of 2' (FIG. 3) displays a distorted octahedral geometry around the ruthenium center, including the ^{t}Bu-PNP, hydride and BH$_4$ units. The hydride ligand is bound to the Ru center cis to the pyridine nitrogen (N1-Ru1-Hru, 81 (2)°, while the BH$_4$ unit is coordinated to Ru(II) center in a $\eta^{2'}$ mode. The two Ru—H bonds to the chelating BH$_4$ unit are not equal (1.67(5) and 1.85(6) Å, respectively), while the corresponding Ru—H bonds in the structure of RuH(BH$_4$)(PMe$_3$)$_3$ (Statler et al.) are of equal length. The difference in the case of 2' is a result of the larger trans effect of hydride relative to that of the pyridinic nitrogen atom. Because of the meridional coordination geometry of the ^{t}Bu-PNP framework and lack of a plane of symmetry involving the P, N, P atoms, the protons of the four tert-butyl and two methylene groups are magnetically inequivalent.

TABLE 22

Selected Bond Distances (Å) and Angles (deg) of Complex 2'			
Ru1-N1	2.123 (3)	Ru1-P1	2.311 (1)
Ru1-P2	2.322 (1)	Ru1-HRu	1.57 (5)
Ru1-HB2	1.67 (5)	Ru1-HB4	1.85 (6)
N1-Ru1-HRu	81 (2)	HRu-Ru1-HB4	166 (2)
P1-Ru1-P2	159.6 (1)	HB2-Ru1-N1	177 (2)
N1-Ru1-P2	83.0 (1)	P1-Ru1-N1	82.5 (1)
P2-Ru1-HRU	79 (2)	HRU-Ru1-P1	85 (2)
HB2-Ru1-HB4	70 (2)	HB3-B1-HB1	113 (3)
HB2-B1-HB4	104 (3)		

Synthesis and Characterization of [RuH(η^2-BH$_4$)(PNN)]4'

The N$_2$-bridged binuclear Ru(II) complex [(RuCl$_2$ (PNN))$_2$](μ-N$_2$) 3' was prepared by the reaction of RuCl$_2$ (PPh$_3$)$_3$ with one equivalent of PNN, employing a similar method to the one used for the preparation of 1. Treatment of 3' with an excess (5 equiv) of NaBH$_4$ in 2-propanol for 12 hrs resulted in the formation of the ruthenium(II) hydrido borohydride complex 4' in excellent yield as indicated by $^{31}P\{^1H\}$ NMR spectroscopy (Scheme 26). The $^{31}P\{^1H\}$ NMR spectrum of 4' shows a singlet peak at 116.7 ppm, representing a downfield shift of 29 ppm relative to 3'. The hydride ligand gives rise to a doublet at –16.24 ppm with J_{PH}=28.0 Hz in the

^{1}H NMR spectrum. The IR spectrum of 4' exhibits two strong bands in the terminal B—H region at 2378 and 2311 cm^{-1} and two bands in the bridging M-H—B region at 2096 and 1956 cm^{-1} similar to the IR spectrum of complex 2', consistent with the bidentate η^2-BH$_4$ binding mode (Marks et al.).

Scheme 32

3'

4'

(P = PBu$^t_2$, N = NEt$_2$)
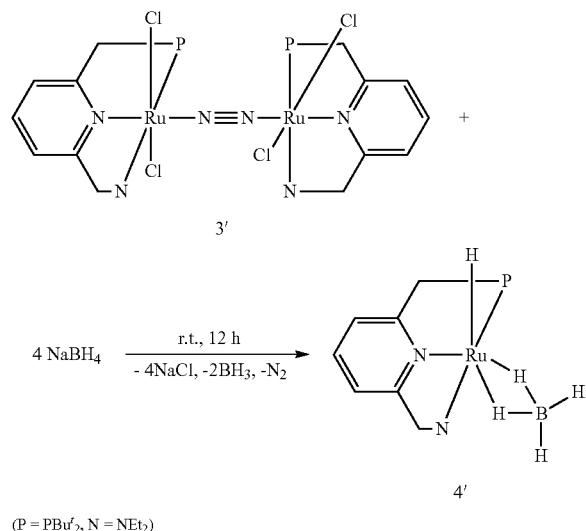
At room temperature, one broad singlet peak at −13.01 ppm is observed in the ^{1}H NMR spectrum of 4' for one proton of BH$_4^-$. A variable-temperature ^{1}H NMR study of 4' in toluene-d$_8$ is shown in FIG. 2, revealing interesting fluxional behavior of the BH$_4^-$ ligand. At 213K, two singlets are observed at −13.21 and −4.33 ppm for the bridging hydrides and two broad singlets at 4.70 and 5.13 ppm for the two terminal hydrides of the BH$_4^-$ ligand, respectively. Upon raising the temperature to 248K, the signals for the two terminal hydrides coalesce while the signal at −4.33 ppm collapses. At 263K, the signals (~5 ppm) for the two terminal hydrides and the signal at −4.33 ppm for one bridging hydride disappear in the baseline and the signal (−13.21 ppm) of another bridging hydride also collapses. Upon temperature increase to 323K, the resonance at −13.21 ppm also disappears into the baseline. Upon raising the temperature to 353K, a very broad singlet peak appears at −2 ppm, indicating that the four hydrides of BH$_4^-$ start to coalesce. The signal of the terminal Ru—H ligand appears as a doublet peak throughout the 213-373K temperature range, indicating that it does not participate in the fluxional process of the BH$_4^-$ ligand. These variable-temperature ^{1}H NMR spectra of complex 4' are similar to those reported for the complexes RuH(BH$_4$)(PMe)$_3$ (Statler et al.) and RuH(BH$_4$)(ttp) (ttp=PhP (CH$_2$CH$_2$CH$_2$PPh$_2$)$_2$) (Letts et al.). The bridging hydride (−4.33 ppm) trans to the terminal Ru—H exchanges positions with the two terminal hydrides on the boron at 263K. These hydrogen atoms further exchange with the bridging hydride (−13.21 ppm) trans to pyridinic nitrogen above 323K and the calculated coalescence frequency at −2.0 ppm was observed at 353K.

Synthesis and Characterization of [RuCl$_2$(PPh$_3$)(^{i}Pr-PNP)] 5 and [RuH(η^1-BH$_4$)(PPh$_3$)(^{i}Pr-PNP)]6'.

Heating of RuCl$_2$(PPh$_3$)$_3$ with one equivalent of ^{i}Pr-PNP (^{i}Pr-PNP=2,6-bis(di-iso-propylphosphinomethyl)pyridine) in THF at 65° C. for 6 hrs resulted in formation of the PPh$_3$

complex 5' in 75% yield (Scheme 27). The ^{31}P $\{$[1]H$\}$ NMR spectrum of 5' exhibits one doublet at 46.4 ppm and one triplet peak at 43.2 ppm, indicating that triphenylphosphine is coordinated to the Ru(II) center, as observed also with the reported Ph-PNP—Ru(II) dichloride complex (Ph-PNP=2,6-bis (diphenylphosphinomethyl)pyridine) (Jia et al.). In contrast, the ^{t}Bu complexes 1' and 3' do not contain coordinated PPh$_3$, under similar preparation conditions, probably because of the steric bulk of the tert-butyl group of ^{t}Bu-PNP and PNN ligands. The two methylene groups of ^{i}Pr-PNP give rise to one triplet peak at 3.92 ppm with J$_{PH}$=4.0 Hz, indicating the existence of a symmetric plane involving the P, N, P atoms. The PPh$_3$ ligand is coordinated to the Ru(II) center trans to the nitrogen atom of ^{i}Pr-PNP and the chloride ligands are coordinated to metal center trans to each other.

In analogy to the preparation of complexes 2' and 4', treatment of complex 5' with excess (2.5 equiv) of NaBH$_4$ in isopropanol at room temperature resulted in precipitation of the Ru(II) hydrido borohydride complex 6' as a yellow solid in 85% yield (Scheme 27). The [31]P$\{$[1]H$\}$ NMR spectrum of 6' exhibits a doublet signal at 61.6 ppm and a triplet signal at 67.9 ppm, corresponding to the two phosphorus atoms of ^{i}Pr-PNP and one phosphorus atom of PPh$_3$, respectively. It is noted that the signal of the PPh$_3$ ligand of 6' is downfield shifted relative to that of ^{i}Pr-PNP, unlike the corresponding signals of complex 5. The Ru—H gives rise in the ^{1}H NMR of 6' to a quartet signal at −14.00 ppm with J$_{PH}$=J$_{P'H}$=28.0 Hz. A broad peak at −0.84 ppm is assigned to the four protons of the BH$_4$ ligand, which is probably coordinated to the Ru(II) center in a η^1 mode, similar to the reported bonding of ruthenium borohydride complexes by Ohkuma et al. and Guo et al. The IR spectrum of 6' exhibits strong absorptions at 2361, 2292 and a strong broad peak at 1884 cm,$^{-1}$ consistent with the monodentate η^1-BH$_4$ bonding mode (Marks et al.).

Scheme 33

RuCl$_2$(PPh$_3$)$_3$ + ^{i}Pr—PNP $\xrightarrow[\text{-2 PPh}_3]{\text{THF, 65° C., 6 hrs}}$

5'

5' + 2 NaBH$_4$ $\xrightarrow[\text{-2NaCl, -BH}_3]{\text{r.t., 12 h}}$

6'
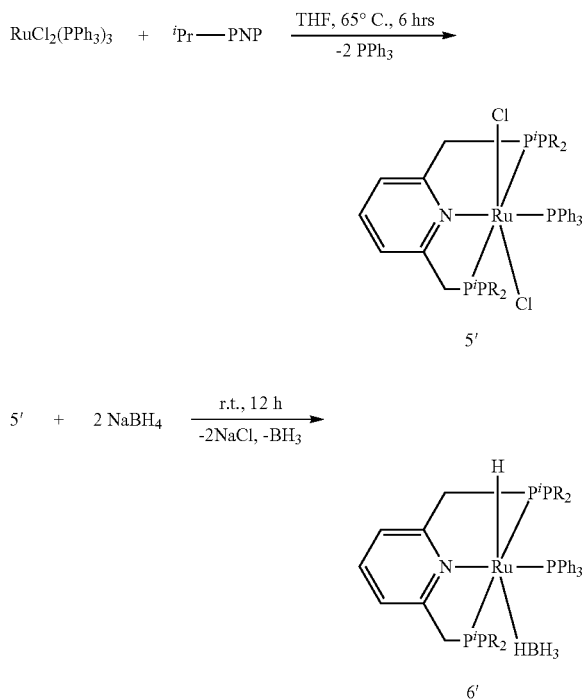
Synthesis of Borohydride Complex 8'

Scheme 34

4

8'
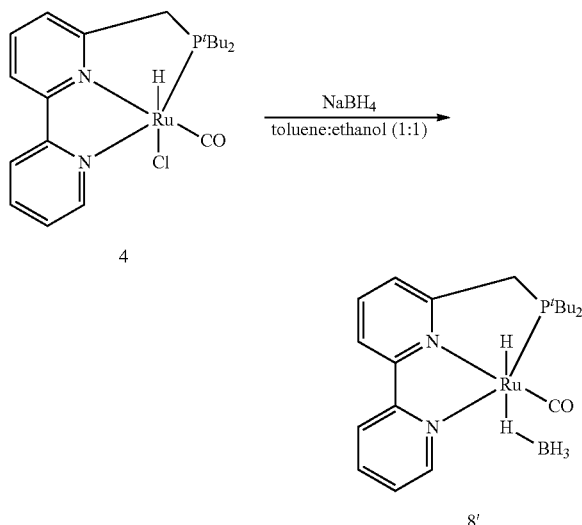
RuHCl(CO)(BPy-^{t}PNN) complex 4 (82 mg, 0.17 mmol) and NaBH$_4$ (32 mg, 0.85 mmol) were placed in a 20 mL Schlenk flask equipped with a Teflon-coated magnetic stirring bar. A 1:1 mixture of toluene and ethanol (4 mL) was added to the flask. It was then stirred at 65° C. for 5 min (to get homogeneous solution) then at room temperature for 2 hr to give a reddish yellow solution. The solvent was removed in vacuo. The resulting residue was dissolved in CH$_2$Cl$_2$ (6 mL) and the remaining insoluble materials were removed by filtration through a Celite pad (0.5 g). The filtrate was concentrated to ca. 0.5 mL and 5 mL of pentane was added to cause precipitation of a orange-yellow solid, which was filtered and dried under vacuum to give 72 mg (92%) of analytically pure RuH(CO)(η^1BH4)BPy-^{t}PNN) complex 8'. ^{31}P $\{^1$H$\}$NMR (202 MHz, CD$_2$Cl$_2$): 110.67 (s). ^{1}H NMR (500 MHz, CD$_2$Cl$_2$): −12.27 (d, ^{2}J$_{PH}$=21.5 Hz, 1H, Ru—H), −2.34--1.90 (br d, 4H, Ru—HBH$_3$), 1.31 (d, J$_{PH}$=13.0 Hz, 9H, P(C(CH$_{a3}$)$_3$), 1.43 (d, J$_{PH}$=13.5 Hz, 9H, P(C(CH$_{b3}$)$_3$), ABX system centred at 3.62 and 3.69 (2H, PCH$_a$H$_b$), 7.41-7.43 (m, 1H, H-5'), 7.56 (d, J$_{HH}$=8.0 Hz, 1H, H-5), 7.85-7.89 (m, 2H, H-4 and H-4'), 7.96 (d, J$_{HH}$=7.5 Hz, 1H, H-3), 8.04 (d, J$_{HH}$=8.0 Hz, 1H, H-3'), 9.12-9.13 (br m, 1H, H-6'). ^{13}C$\{^1$H$\}$NMR (125 MHz, CD$_2$Cl$_2$): 28.43 (d, J$_{PC}$=3.8 Hz, P(C(C$_a$H$_3$)$_3$), 29.63 (d, J$_{PC}$=3.8 Hz, P(C(C$_b$H$_3$)$_3$), 35.87 (d, J$_{PC}$=16.3 Hz, P(C$_{a/b}$ (CH$_3$)$_3$), 37.34 (d, J$_{PC}$=16.3 Hz, PCH$_2$), 119.26 (s, C-3), 121.16 (s, C-3'), 122.53 (d, J$_{PC}$=8.8 Hz, C-5), 125.71 (s, C-5'), 135.97, (s, C-4'), 137.07 (s, C-4), 153.69 (s, C-6'), 154.79 (br s, C-2), 155.91 (s, C-2'), 163.95 (d, J$_{PC}$=3.78 Hz, C-6), 206.90 (br d, J$_{PC}$=15 Hz, Ru—CO). IR (KBr disc, CH$_2$Cl$_2$): 2313 (B—H stretching), 1988 (Ru—H stretching), 1046 (BH$_3$ deformation), 1019 (BH$_3$ deformation). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC.

Dehydrogenation of Alcohols Using Complexes 2', 4', 6' and 8' as Catalysts.

As some of the inventors of the present invention have demonstrated (Zhang 2004, Zhang 2005), PNP and PNN Ru(II) complexes catalyze the dehydrogenation of secondary alcohols to ketones and primary alcohols to esters. It has now been discovered that the ruthenium hydrido borohydride complexes of 2', 4', and 6' and 8' catalyze the dehydrogenation of alcohols under base-free conditions and in absence of

hydrogen acceptors. Indeed, when complex 2' was heated with 1000 equivalents of 1-phenyl-1-ethanol in toluene for 24 hrs, 28.6% of the alcohol were converted to acetophenone, accompanied by the evolution of hydrogen gas (Table 23, entry 1). Similarly, upon heating of 1-phenyl-1-ethanol with 0.1% 4' or 6' in toluene for 24 hrs, acetophenone was formed in 86.5% and 76.5% yield, respectively (Table 23, entry 2 and 3), indicating that the catalytic activity of 4' was significantly higher than that of complexes 2' and 6', probably as a result of the potentially "hemilabile" amine arm of 4', which can play an important role in the catalytic cycle (Zhang 2005). A longer reaction time resulted in a higher yield of the ketone (Table 23, entry 4). Other secondary alcohols can also be dehydrogenated to the corresponding ketones using 4' as catalyst in good yields (Table 23, entries 5-8). The catalysis by 4' was quite sensitive to the reaction temperature, and when 2-propanol was heated at 83° C. with 0.1% 4', acetone was formed in only 12.6% yield after 48 hrs (TON=126), while when heated in toluene at 105° C., 89.9% of acetone were formed during the same reaction period (TON=899).

TABLE 23

Dehydrogenation of secondary alcohols to the corresponding ketones with complexes 2', 4', 6' as catalysts

entry	Cat.	Alcohol	Temp. (° C.)	Time (h)	Conversion (%)	Yield of ketone (%)^a
1	2'	1-phenyl-1-ethanol	115	24	28.6	28.6
2	4'	1-phenyl-1-ethanol	115	24	86.5	86.5
3	6'	1-phenyl-1-ethanol	115	24	77	76.5
4	4'	1-phenyl-1-ethanol	115	48	93	93
5	4'	2-hexanol	115	48	83.2	83
6	4'	2-butanol	110	48	88.8	88.7
7	4'	cyclohexanol	115	48	56.5	56.5
8	4'	2-propanol	105	48	90	89.9
9	4'	2-propanol	83^b	48	12.6	12.6

^{a}reaction conditions: catalyst 0.01 mmol, alcohol 10 mmol, toluene 2 mL, reflux under argon flow

^{b}reflux in neat 2-propanol under argon.

In comparison to the dehydrogenation of secondary alcohols to the corresponding ketones, homogeneous systems capable of dehydrogenation of primary alcohols to the corresponding aldehydes or esters are very rare (Zhang 2005, Murahashi et al., Blum et al., Lin et al. and Zhao et al), probably because of decarbonylation of the product (or intermediate) aldehyde to form an inactive carbonyl complex.

When a toluene solution of benzyl alcohol and 0.1% complex 2' was refluxed for 24 hrs in an open system, benzyl benzoate was formed in 70% yield, accompanied by a small amount of benzaldehyde (4%) (Table 24, entry 1). Refluxing 1-hexanol with 0.1% 2 in toluene (115° C.) or neat (157° C.) for 24 hrs resulted in formation of 60-70% of hexyl hexanoate, accompanied by 2.5-10% hexanal (Table 24, entries 2 and 3). Complex 6' was slightly less catalytically active than 2 (Table 24, entry 7). The PNN complex 4' exhibited significantly higher catalytic activity than that of the PNP complexes 2' and 6'; benzyl alcohol, 1-hexanol and 1-butanol were dehydrogenated to the corresponding esters in over 90% yield after heating with 0.1% 4' in toluene (Table 24, entry 4-6).

TABLE 24

Dehydrogenation of primary alcohols to esters and aldehydes with complexes 2', 4', 6' as catalysts

entry	Cat.	Alcohol	Temp. (° C.)	Conversion (%)	Yield of Aldehyde (%)	Yield of ester (%)[a]
1	2'	benzyl alcohol	115	75	4	70
2	2'	1-hexanol	115	72	2.5	69
3	2'	1-hexanol	157[a]	70	10	59.4
4	4'	benzyl alcohol	115	99	0	99
5	4'	1-hexanol	115	94	0	94
6	4'	1-butanol	110	96	0.2	95.5
7	6'	benzyl alcohol	115	62	3.4	58.6
8	6'	1-hexanol	157[b]	57.5	9.5	47.4

[a]reaction conditions: catalyst 0.01 mmol, alcohol 10 mmol, toluene 2 mL heated under reflux for 24 hrs under argon flow

[b]reflux in neat 1-hexanol under argon flow

Dehydrogenation of Alcohols to Esters Using Complex 8' as Catalyst

Scheme 35

$$2 \ R{\sim}OH \xrightarrow[\text{Toluene, reflux, 5 hr}]{\substack{\text{complex 8'} \\ \text{0.01 mmol}}} R{\sim}\underset{O}{\overset{O}{C}}{\sim}O{\sim}R \ + \ 2H_2$$

10.0 mmol
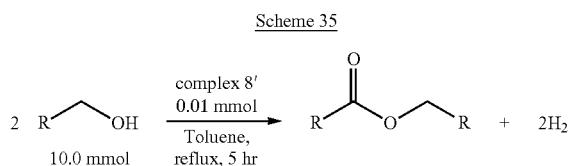
TABLE 25

Dehydrogenation of alcohols to esters using complex 8' as catalyst

Entry	Alcohols	Esters	Conv. (%)	Yield (%)[a]
1	1-Hexanol	Hexyl hexanoate	99.8	99.0
2	Benzyl alcohol	Benzyl benzoate	~100	99.3

[a]Complete conversion of alcohol was observed and no formation of aldehyde (by GC).

Amidation Using Complex 4' as a Catalyst

Scheme 36

-continued

toluene,
120° C., 18 hrs
conversion = 100%

isolated yield: 98%
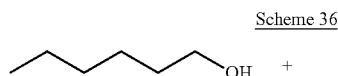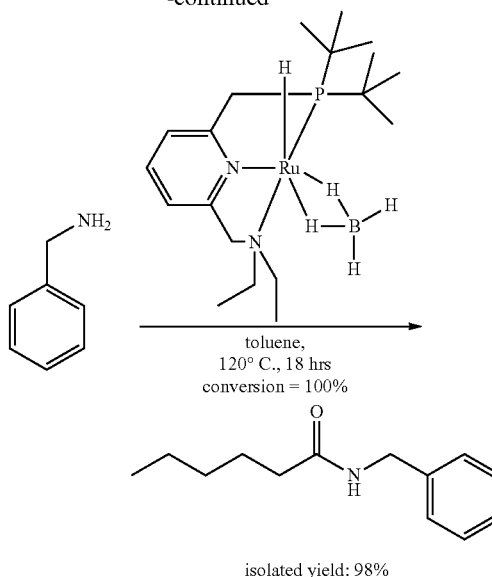
Complex 4' (4.4 mg, 0.01 mmol), 1-hexanol (1.02 g, 10 mmol), benzyl amine (1.07 g, 10 mmol) and toluene (3 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 18 h. After cooling to room temperature, the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system and shows that 100% conversion of the 1-hexanol. To the reaction mixture, hexane (30 mL) was added to precipitate out the N-benzylhexanamide as white coloured solid and filtered off the solid to get the pure product in 98% yield.

Amidation Using Complex 8' as Catalyst

Scheme 37

$$R{\sim}OH \ + \ R_2{\sim}NH_2 \xrightarrow[\text{Toluene, reflux, Ar flow, 14 hrs}]{\substack{\text{complex 8'} \\ \text{0.01 mmol}}} R_1{\sim}\underset{O}{\overset{O}{C}}\underset{H}{N}{\sim}R_2 \ + \ 2H_2$$

10 mmol   10 mmol
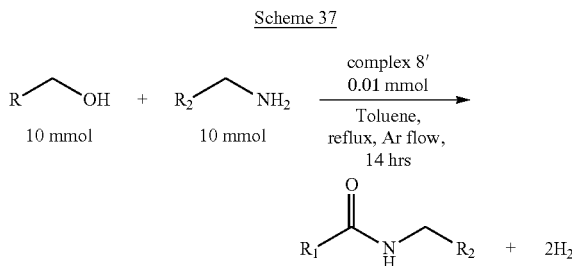
TABLE 26

Amidation using complex 8' as a catalyst

Entry	Alcohols	Amines	Amides	Yield (isolated)
1	HO${\sim}(\ )_4$			59[a]

TABLE 26-continued

Amidation using complex 8' as a catalyst

Entry	Alcohols	Amines	Amides	Yield (isolated)
3				71[b]

[a]Conversion of alcohol is 87.8%. Other products are Ester (5.2%) and Imine (17%) also formed (by GC).
[b]Conversion of alcohol is 91.1%. Other products are Ester (3.5%) and Imine (12%) also formed (by GC).

Ester Hydrogenation Using Complexes as Catalysts

Scheme 38
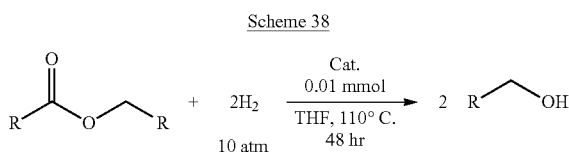
TABLE 27

Ester hydrogenation

Entry	Cat.	Esters	Alcohols	Conv. (%)	Yield (%)
1	8'	Hexyl hexanoate (2 mmol)	1-Hexanol	99.8	98.9
2	8'	Methyl formate (15 mmol)	MeOH	96.5	94.7
3	4'	Hexyl hexanoate (2 mmol)	1-Hexanol	~100	99.4
4	4'	Butyl butyrate (2 mmol)	1-Butanol	~100	98.0
5	6'	Butyl butyrate (2 mmol)	1-Butanol	9.8	9.0

Dehydrogenation of diols to the corresponding lactones catalyzed by complexes 2' and 4'[a]

TABLE 28

Dehydrogenation of esters to lactones

entry	cat.	diol	Lactone yield (%)[b]
1	2'		(33)
2	4'		(72)

TABLE 28-continued

Dehydrogenation of esters to lactones

entry	cat.	diol	Lactone yield (%)[b]
3	4'		(81)
4	4'		(86)
5	4'		(90) and 76[c]

[a]Reaction conditions: catalyst (0.01 mmol), diol (3 mmol) and 2 mL of toluene were refluxed in an open system under argon for 48 hrs.
[b]Yields of the lactones were analyzed by ^{1}H NMR of the reaction mixture.
[c]Isolated yield.

General procedure for the catalytic dehydrogenation of diols to lactones. Complexes 2' or 4' (0.01 mmol), diol (3 mmol), and toluene (2 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 48 hrs. After cooling to room temperature, the yield of the lactones was determined by ^{1}H NMR spectroscopy from the reaction mixture. The resulting mixture was concentrated in vacuo for about 3-4 h. The purification was performed on silica gel column using hexane-ethylacetate mixture as eluent. The products were analyzed by ^{1}H NMR and the spectra were identical with the authentic samples.

Example 10

Experimental Section—Borohydride Complexes

General Procedures

All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box equipped with

a MO 40-2 inert gas purifier or using standard Schlenk techniques. All solvents were reagent grade or better. All non-deuterated solvents were refluxed over sodium/benzophenone ketyl and distilled under argon atmosphere. Deuterated solvents were used as received. All solvents were degassed with argon and kept in the glove box over 4 Å molecular sieves. Complexes 1' and 3' were prepared as reported previously (Zhang 2004, Milstein). ^{i}Pr-PNP (2,-6-bis-(di-iso-propylphosphinomethyl)pyridine) (Jansen et al.), $RuCl_2(PPh_3)_3$, (Holm et al.) were prepared according to literature procedures.

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at 400 or 500, 100 or 126, and 162 or 202 MHz, respectively, using a Bruker AMX-400 and AMX-500 NMR spectrometers. ^{1}H and ^{13}C{^{1}H} NMR chemical shifts are reported in ppm downfield from tetramethylsilane. ^{31}P NMR chemical shifts are reported in parts per million downfield from H_3PO_4 and referenced to an external 85% solution of phosphoric acid in D_2O. Abbreviations used in the NMR follow-up experiments: b, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, v, virtual. Elemental analyses were performed at Kolbe Laboratorium, Mulheim, Germany.

Synthesis of [RuH(BH$_4$)(^{t}Bu-PNP)] 2'.

To a suspension of complex 1' (58 mg, 0.05 mmol) in 2-propanol (10 ml) was added a very fine powder of $NaBH_4$ (9.5 mg, 0.25 mmol), and the mixture was stirred at room temperature for 12 hrs. The mixture was filtered and the orange filtrate was taken to dryness under vacuum. The residue was extracted with diethyl ether (3×5 mL). The ether solution was evaporated under vacuum to yield complex 2' as an orange solid. The complex was dried under vacuum overnight. Yield: 50 mg (98%).

^{31}P{^{1}H} NMR (C_6D_6): 86.3 (s); ^{1}H NMR (C_6D_6): −16.09 (t, 1H, J_{PH}=18.0 Hz, Ru—H), −16.01 (br s, 1H, BH$_4$), −4.48 (br s, 1H, BH$_4$), 1.45 (t, 18H, J_{PH}=6.0 Hz, P(C(CH$_3$)$_3$)), 1.56 (t, 18H, J_{PH}=6.0 Hz, P(C(CH$_3$)$_3$)$_2$), 3.08 (dt, 2H, J_{HH}=16.0 Hz, J_{PH}=4.0 Hz, —CHHP), 3.19 (dt, 2H, J_{HH}=16.0 Hz, J_{PH}=4.0 Hz, —CHHP), 5.49 (br s, 2H, BH$_4$), 6.52 (d, 2H, J_{HH}=8.0 Hz, pyridine-H3, H5), 6.76 (t, 1H, J_{HH}=8.0 Hz, pyridine-H4). ^{13}C {^{1}H} NMR(C_6D_6): 29.7 (s, P(CH(CH$_3$)$_2$)$_2$), 30.2 (s, P(C(CH$_3$)$_3$)$_2$), 35.0 (t, J_{PC}=6.5 Hz, P(C(CH$_3$)$_3$)$_2$), 35.6 (t, J_{PC}=5.0 Hz, P(C(CH$_3$)$_3$)$_2$), 39.0 (t, J_{PC}=7.0 Hz, CH$_2$P), 118.2 (t, J_{PC}=4.0 Hz, pyridine-C3, C5), 131.0 (s, Pyridine-C4), 165.1 (t, J_{PC}=4.5 Hz, Pyridine-C2, C6).

IR (KBr pellets): 2395, 2327, 2104, 2024, 1461, 1184 cm^{-1}.

Anal. Calcd. for $C_{23}H_{48}BNP_2Ru$: C, 53.90; H, 9.45. Found: C, 53.86; H, 9.49.

Synthesis of [RuH(BH$_4$)(PNN)] 4'.

To a suspension of complex 3' (51 mg, 0.05 mmol) in 2-propanol (10 ml) was added a very fine powder of $NaBH_4$ (9.5 mg, 0.25 mmol), and the mixture was stirred at room temperature for 12 hrs. The mixture was filtered and the orange filtrate was taken to dryness under vacuum. The orange solid residue was extracted with diethyl ether (3×5 mL). The ether solution was evaporated under vacuum yielding complex 4' as a red-orange solid, which was dried under vacuum overnight. Yield: 40 mg (91%).

^{31}P{^{1}H} NMR (C_6D_6): 116.7 (s); ^{1}H NMR (C_6D_6, 298 K): −16.24 (t, 1H, J_{PH}=28.0 Hz, Ru—H), —13.10 (Br s, 1H, BH$_4$), 0.84 (t, 3H, J_{HH}=6.0 Hz, N(CH$_2$CH$_3$)$_2$), 0.99 (t, 3H, J_{HH}=6.0 Hz, N(CH$_2$CH$_3$)$_2$), 1.28 (d, 9H, J_{PH}=12.0 Hz, P(C(CH$_3$)$_3$)), 1.43 (d, 9H, J_{PH}=12.0 Hz, P(C(CH$_3$)$_3$)$_2$), 2.31 (m, 1H, N(CH$_2$CH$_3$)$_2$), 2.49 (m, 1H, N(CH$_2$CH$_3$)$_2$), 2.71 (dd, 1H, J_{HH}=16.0 Hz, J_{PH}=8.0 Hz, —CHHP), 2.98 (dd, 1H, J_{HH}=16.0 Hz, J_{PH}=12.0 Hz, —CHHP), 3.05 (m, 1H, N(CH$_2$CH$_3$)$_2$), 3.41 (d, 1H, J_{HH}=14.0 Hz, NCHH-py), 3.54 (d, 1H, J_{HH}=14.0 Hz, NCHH-py), 3.73 (m, 1H, N(CH$_2$CH$_3$)$_2$), 6.30 (d, 1H,

J_{HH}=8.0 Hz, pyridine-H5), 6.51 (d, 1H, J_{HH}=8.0 Hz, pyridine-H3), 6.71 (t, 1H, J_{HH}=8.0 Hz, pyridine-H4). ^{1}H NMR (Toluene-d$_8$, 243 K): −16.30 (t, 1H, J_{PH}=28.0 Hz, Ru—H), −13.21 (Br s, 1H, BH$_4$), −4.33 (br s, 1H, BH$_4$), 0.71 (br s, 3H, N(CH$_2$CH$_3$)$_2$), 0.92 (br s, 3H, N(CH$_2$CH$_3$)$_2$), 1.18 (d, 9H, J_{PH}=12.0 Hz, P(C(CH$_3$)$_3$)), 1.35 (d, 9H, J_{PH}=12.0 Hz, P(C(CH$_3$)$_3$)$_2$), 2.10 (m, 1H, N(CH$_2$CH$_3$)$_2$), 2.31 (m, 1H, N(CH$_2$CH$_3$)$_2$), 2.53 (dd, 1H, J_{HH}=16.0 Hz, J_{PH}=8.0 Hz, —CHHP), 2.82 (dd, 1H, J_{HH}=16.0 Hz, J_{PH}=8.0 Hz, —CHHP), 2.93 (br m, 1H, N(CH$_2$CH$_3$)$_2$), 3.15 (d, 1H, J_{HH}=16.0 Hz, NCHH-py), 3.33 (d, 1H, J_{HH}=16.0 Hz, NCHH-py), 3.37 (m, 1H, N(CH$_2$CH$_3$)$_2$), 4.69 (br s, 1H, BH$_4$), 5.00 (br s, 1H, BH$_4$), 6.16 (d, 1H, J_{HH}=8.0 Hz, pyridine-H5), 6.38 (d, 1H, J_{HH}=8.0 Hz, pyridine-H3), 6.62 (t, 1H, J_{HH}=8.0 Hz, pyridine-H4). ^{13}C{^{1}H} NMR (C_6D_6): 8.8 (s, N(CH$_2$CH$_3$)$_2$), 11.0 (s, N(CH$_2$CH$_3$)$_2$), 29.0 (d, J_{PC}=4.0 Hz, P(C(CH$_3$)$_3$)$_2$), 34.2 (d, J_{PC}=15.1 Hz, P(C(CH$_3$)$_3$)$_2$), 37.0 (d, J_{PC}=10.0 Hz, P(C(CH$_3$)$_3$)$_2$), 38.9 (d, J_{PC}=19.1 Hz, PCH$_2$—), 51.1 (s, N(CH$_2$Me)$_2$), 51.2 (s, N(CH$_2$Me)$_2$), 63.7 (s, py-CH$_2$N), 117.5 (s, Py-C3), 118.5 (s, Py-05), 128.8 (s, Py-C4), 159.9 (s, Py-C6), 163.7 (d, J_{PC}=4.0 Hz, py-C2).

IR (KBr pellets): 2378, 2311, 2096, 1956, 1469, 1177 cm^{-1}.

Anal. Calcd. for $C_{19}H_4OBN_2PRu$: C, 51.93; H, 9.18. Found: C, 51.86; H, 9.24.

Synthesis of [RuCl$_2$(PPh$_3$)(^{i}Pr-PNP)] 5'.

To a suspension of Ru(PPh$_3$)$_3$Cl$_2$ (480 mg, 0.5 mmol) in dry THF (20 ml) was added ^{i}Pr-PNP (170 mg, 0.5 mmol) and the mixture was stirred and heated at 65° C. for 6 hrs. The yellow solution was concentrated to 4 mL under vacuum and 20 mL of pentane were added to precipitate a yellow solid. The solid was isolated by filtration, washed with pentane (3×2 mL) and dried under vacuum to give 290 mg (75% yield) of 5 as a yellow solid.

^{31}P NMR (CD$_2$Cl$_2$): 46.4 (d, J_{PP}=27.5 Hz), 43.2 (t, J_{PP}=27.5 Hz). ^{1}H NMR (CD$_2$Cl$_2$): 0.87 (q, 12H, J_{PH}=J_{HH}=8.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 1.13 (q, 12H, J_{PH}=J_{HH}=8.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 2.43 (m, 4H, P(CH (CH$_3$)$_2$)$_2$), 3.92 (t, 4H, J_{PH}=4.0 Hz, —CH$_2$P), 7.26 (m, 9H, P(C$_6$H$_5$)$_3$), 7.30 (d, 2H, J_{HH}=8.0 Hz, pyridine-H3, 5), 7.53 (t, 1H, J_{HH}=8.0 Hz, pyridine-H4), 7.91 (m, 6H, P(C$_6$H$_5$)$_3$). ^{13}C{^{1}H} NMR (CD$_2$Cl$_2$): 19.6 (s, P(CH(CH$_3$)$_2$)$_2$), 20.7 (s, P(CH(CH$_3$)$_2$)$_2$), 25.1 (t, J_{PC}=8.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 38.9 (t, J_{PC}=10.1 Hz, CH$_2$P), 119.9 (s, Py-C3,5), 127.2 (d, J_{PC}=9.0 Hz, m-C$_6$H$_5$—P), 128.8 (s, p-C$_6$H$_5$—P), 135.0 (d, J_{PC}=9.0 Hz, o-C$_6$H$_5$—P), 136.7 (s, Py-C4), 140.4 (d, J_{PC}=36.2 Hz, ipso-C$_6$H$_5$—P), 164.8 (t, J_{PP}=4.0 Hz, py-C2,6).

Anal. Calcd. for $C_{37}H_{50}NP_3Cl_2Ru$: C, 57.44; H, 6.52. Found: C, 57.28; H, 6.53.

Synthesis of [RuH(BH$_4$)(PPh$_3$)(^{i}Pr-PNP)] 6'.

To a suspension of complex 5 (77 mg, 0.1 mmol) in 2-propanol (10 ml) was added a fine powder of $NaBH_4$ (9.5 mg, 0.25 mmol). The mixture was stirred at room temperature for 12 hrs and then filtered. The resulting yellow solid was washed with 2-propanol (3×1.5 mL) and then dissolved in benzene (10 mL) and the solution was filtered. The yellow filtrate was evaporated to dryness under vacuum, yielding complex 6' as a yellow solid which was dried under vacuum overnight to give 61 mg (85% yield). ^{31}P{^{1}H} NMR (C_6D_6): 61.6 (d, J_{PP}=29.2 Hz), 67.9 (t, J_{PP}=29.2 Hz). ^{1}H NMR (C_6D_6): −14.0 (q, 1H, J_{PH}=28.0 Hz, Ru—H), −0.84 (br s, 4H, BH$_4$), 0.91 (q, 6H, J_{PH}=J_{HH}=8.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 0.87 (m, 12H, J_{PH}=J_{HH}=8.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 1.18 (q, J_{PH}=J_{HH}=8.0 Hz, 6H, P(CH(CH$_3$)$_2$)$_2$), 1.44 (m, 2H, P(CH (CH$_3$)$_2$)$_2$), 1.77 (m, 2H, P(CH(CH$_3$)$_2$)$_2$), 2.85 (dt, 2H, J_{HH}=16.0 Hz, J_{PH}=4.0 Hz, –CHHP), 3.92 (dt, 2H, J_{HH}=16.0 Hz, J_{PP}=4.0 Hz, —CHHP), 6.56 (d, 2H, J_{HH}=8.0 Hz, pyridine-H3, 5), 6.79 (t, 1H, J_{HH}=8.0 Hz, pyridine-H4), 7.01 (d, 3H, J_{HH}=8.0 Hz, P(C$_6$H$_5$)$_3$), 7.12 (t, 6H, J_{HH}=8.0 Hz, P(C$_6$H$_5$)$_3$), 8.18 (t, 6H, J_{HH}=8.0 Hz, P(C$_6$H$_5$)$_3$). ^{13}C{^{1}H}

NMR (C$_6$D$_6$): 18.0 (s, P(CH(CH$_3$)$_2$)$_2$), 18.5 (s, P(CH (CH$_3$)$_2$)$_2$), 19.6 (s, P(CH(CH$_3$)$_2$)$_2$), 20.8 (s, P(CH(CH$_3$)$_2$)$_2$), 25.6 (t, J$_{PC}$=8.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 26.4 (t, J$_{PC}$=11.6 Hz, CH$_2$P), 39.2 (t, J$_{PC}$=6.0 Hz, P(CH(CH$_3$)$_2$)$_2$), 118.4 (t, J$_{PC}$=2.5 Hz, Py-C3,5), 127.1 (d, J$_{PC}$=9.0 Hz, m-C$_6$H$_5$—P), 128.8 (s, p-C$_6$H$_5$—P), 134.2 (s, Py-C4), 135.7 (d, J$_{PC}$=10.1 Hz, o-C$_6$H$_5$—P), 142.0 (d, J$_{PC}$=36.2 Hz, ipso-C$_6$H$_5$—P), 163.7 (t, J$_{PC}$=4.5 Hz, py-C2,6).

IR (KBr pellet): 2361, 2293, 2246, 1884, 1458, 1060 cm^{-1}.

Anal. Calcd. for C$_{37}$H$_{55}$BNP$_3$Ru: C, 61.84; H, 7.72. Found: C, 61.98; H, 7.66.

Typical Procedures for the Catalytic Dehydrogenation of Alcohols

(a) Complexes 2' (0.01 mmol), 4' (0.01 mmol) or 6' (0.01 mmol) were dissolved in the neat primary or secondary alcohol (10 mmol). The flask was equipped with a condenser and the solution was heated with stirring in an open system under argon at the specified temperature and time (Tables 18 and 19). After cooling to room temperature, the product aldehydes, esters or ketones were determined by GC, using mesitylene or (in the case of 1-butanol) benzene as internal standards, employing a Carboxen 1000 column on a HP 690 series GC system.

(b) A solution containing the catalyst (0.01 mmol) (complexes 2', 4' or 6') and the alcohol (10 mmol) in toluene (2 mL) was heated in a flask equipped with a reflux condenser under argon in an open system at the specified temperatures and times (Tables 2 and 3). After cooling to room temperature, the products were determined by GC using mesitylene or benzene (for 1-butanol) as internal standards, employing a Carboxen 1000 column on a HP 690 series GC system.

X-Ray Crystal Structure Determination of 2'.

The crystal was mounted on a nylon loop and flash frozen in a nitrogen stream at 120K. Data were collected on a Nonius Kappa CCD diffractometer mounted on a FR590 generator equipped with a sealed tube with Mo Kα radiation (λ=0.71073 Å) and a graphite monochromator. The four structures were solved using direct methods with SHELXS-97 based on F^2.

Complex 2':

C$_{23}$H$_{48}$BNP$_2$Ru, yellow plate, 0.40×0.40×0.30 mm^3, monoclinic, P2$_I$ (No. 4), a=12.541 (3) Å, b=15.314 (3) Å, c=15.131 (3) Å, β=111.85 (3)°, V=2697.3 (9) Å^3, Z=4, fw=512.4, F(000)=1088, D$_c$=1.262 Mg/m^3, μ=0.709 mm^{-1}. The final cycle of refinement based on F^2 gave an agreement factor R=0.027 for data with I>2σ(I) and R=0.030 for all data (6375 reflections) with a goodness-of-fit of 1.080. Idealized hydrogen atoms were placed and refined in the riding mode, with the exception of Hru and Hb1-Hb4 which were located in the difference map and refined independently.

Example 11

Synthesis of Complex 9 and Catalysis by It

Scheme 39

1) KO^{t}Bu
2) (^{t}Bu)$_2$PCl

Ether, 0° C.

-continued

RuHCl(PPh$_3$)$_3$(CO)

THF, 65° C., 12 hr
-3 PPh$_3$

BPy——(Ph)PNN

9
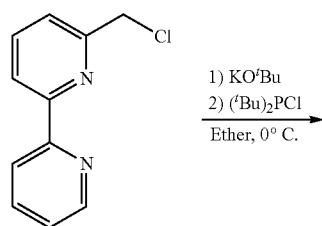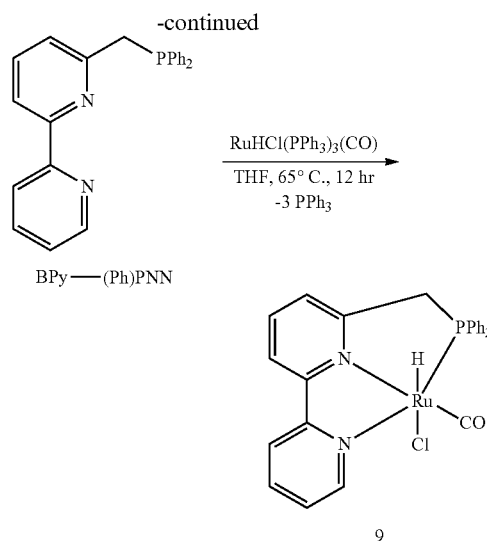
(a) Synthesis of the Ligand BPy-(Ph)PNN (10)

An oven-dried 250 mL three-necked round bottom flask equipped with an argon inlet, a stirring bar, dropping funnel and one rubber septum was cooled under a stream of argon. The flask was then charged with chlorodiphenylphosphine (1.08 g, 6 mmol) in 30 mL dry ether. The solution was cooled to 0° C. and a THF solution (5 mL) of potassium tert-butoxide (74 mg, 6.6 mmol) was added dropwise via syringe during 10 min. The resulting brown coloured mixture was stirred for 1 hr at 0° C. and then a solution of 6-chloromethyl-2,2'-bipyridine (1.02 g, 5 mmol) in 20 mL dry ether was added dropwise (~15 min) to it. The stirring was continued for a further 1 hr at the same temperature and the mixture was allowed to slowly warm up to room temperature and stirred overnight. To this reaction mixture was added 20 mL of degassed water and the ether phase was separated under N$_2$ atmosphere. The aqueous phase was extracted with ether (2×20 mL). The combined ether solutions were dried over anhydrous Na$_2$SO$_4$, filtered under N$_2$ pressure, and the solvent was removed under vacuum to get brownish-white solid. This was purified by column chromatography in the nitrogen glove box (basic alumina; hexane:ether (10:1) as eluent) to yield 1.08 g (61%) of 6-di-phenyphosphinomethyl-2,2'-bipyridine (BPy-(Ph) PNN) as a white crystalline solid.

^{31}P {1H}NMR (122 MHz, CD$_2$Cl$_2$): −8.28 (s). ^{1}H NMR (300 MHz, CD$_2$Cl$_2$): 3.81 (s, 2H, P—CH2), 7.13 (d, JHH=7.5 Hz, 1H, H-5), 7.32 (ddd, JHH=7.5 Hz, JHH=4.8H, JPH=1.2 Hz, 1H, H-5'), 7.40-7.45 (m, 6H, Ph-H), 7.58-7.63 (m, 4H, Ph-H), 7.69 (t, JHH=7.8 Hz, 1H, H-4), 7.80 (dt, JHH=7.8 Hz, JHH=2.1 Hz, 1H, H-4'), 8.28 (br d, JHH=8 Hz, 2H, H-3 and 11-3'), 8.68-8.70 (m, 1H, H-6'). ^{13}C{1H}NMR (125 MHz, CD2Cl2): 38.35 (d, JPC=16.3 Hz, P—CH2), 118.07 (s, C-3), 121.02 (s, C-3'), 123.55 (s, C-5'), 123.61 (d, JPC=8.4 Hz, C-5), 128.34 (s, Ph-C), 128.40 (Ph-C), 128.65 (s, Ph-C), 132.90 (s, Ph-C), 133.05 (s, Ph-C), 136.61, (s, C-4'), 136.97 (s, C-4), 138.72 (d, JPC=15.0 Hz, Ph-C(quar)), 149.02 (s, C-6'), 155.49 (s, C-2), 156.22 (s, C-2'), 157.64 (d, JPC=7.5, C-6). Anal. Calcd. for C$_{23}$H$_{19}$N$_2$P: C, 77.95; H, 5.40. Found: C, 78.13; H, 5.61. MS (ESI, MeOH): 355 (100%, M+1)+). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC.

(b) Synthesis of Complex 9

To an oven dried 25 mL pressure vessel equipped with magnetic stirring bar was added ligand, BPy-(Ph)PNN (10)

(148 mg, 0.42 mmol), RuHCl(CO)(PPh$_3$)$_3$ (382 mg, 0.4 mmol), and 8 mL dry THF in a nitrogen glove box. The flask was sealed and heated at 65° C. for 12 hr with stirring outside the glove box, then cooled to room temperature to lead to reddish-brown solid. It was reintroduced to the glove box, and the solvent was decanted and the solid thus obtained was washed with ether (3×5 mL), then dried under vacuum to give analytically pure complex RuHCl(CO)(BPy-(Ph)PNN) (184 mg, 84%). ^{31}P{1H}NMR (202 MHz, CD$_2$Cl$_2$): 69.44 (s). ^{1}H NMR (500 MHz, CD$_2$Cl$_2$): −14.09 (d, JPH=25.5 Hz, 1H, Ru—H), 4.38-4.50 (m, 2H, P—CH2), 7.39-7.40 (m, 3H, Ph-H), 7.46-7.51 (m, 4H, Ph-H), 7.60-7.64 (m, 3H, Ph-H), 7.87-7.90 (m, 2H, H-5 and H-5'), 7.57 (d, JHH=7.8 Hz, 1H, H-5), 7.93-7.97 (m, 2H, H-4 and H-4'), 8.04 (d, JHH=8.0 Hz, 1H, H-3), 8.10 (d, JHH=8.0 Hz, 1H, H-3'), 9.22 (br s, 1H, H-6'). ^{13}C{1H}NMR (125 MHz, CD2Cl2): 45.52 (d, JPC=26.3 Hz, P—CH2), 120.04 (s, C-3), 122.65 (s, C-3'), 123.09 (d, JPC=11.3, C-5), 126.21 (s, C-5'), 128.16 (s, Ph-C), 128.24 (s, Ph-C), 128.28 (s, Ph-C), 128.37 (s, Ph-C), 129.82 (s, Ph-C), 130.37 (s, Ph-C), 131.60 (d, JPC=11.3 Hz, Ph-Ca (ortho)), 133.46 (d, JPC=11.3 Hz, Ph-Cb(ortho)), 133.78 (d, JPC=43.8 Hz, Ph-Cb(quar)), (136.64, (s, C-4'), 137.39 (s, C-4), 139.86 (d, JPC=50.0 Hz, Ph-Ca(quar)), 153.39 (s, C-6'), 154.67 (s, C-2), 156.05 (s, C-2'), 160.04 (d, JPC=6.3, C-6). 206.53 (d, JPC=7.5 Hz, Ru—CO). IR (KBr, pellet): 1915 (vCO) cm^{-1}. MS (ESI, CH3CN): 519 (100%, (M−1)$^+$) and MS (ESI, CH$_3$OH): 485 (100%, (M-Cl)$^+$).

Some Examples of Reactions Catalyzed by Complex 9:

Scheme 40
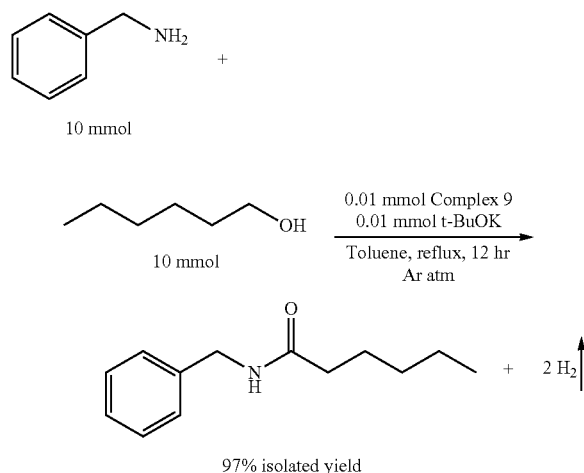
Scheme 41
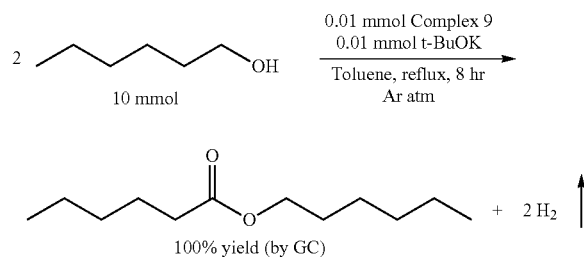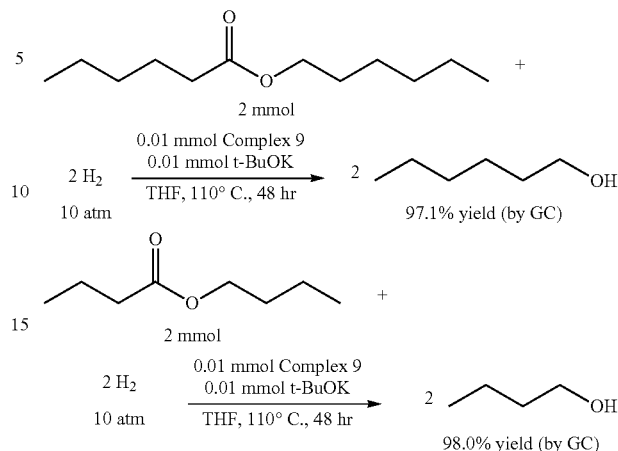
Scheme 42

Example 12

Direct Synthesis of Amides from Esters using Ruthenium-Pincer Catalyst With Liberation of H$_2$ Under Neutral Conditions

PNN-type pincer ruthenium complexes used for catalytic conversion of esters and amines into amides:

Scheme 43
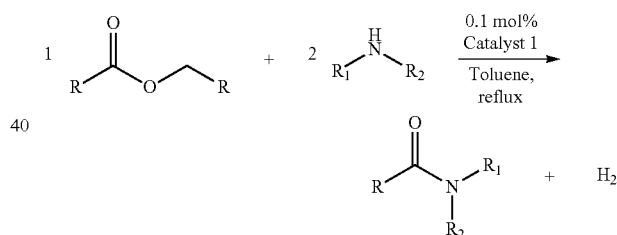
The applicants of the present invention have discovered that amide synthesis from esters and amines can be achieved using the ruthenium PNN catalyst 1. The reaction is general, efficient, environmentally benign and atom economical. It proceeds under neutral conditions without acid/base/activators/promoters. Notably, this reaction affords with amide in high TON (1000) and H$_2$ as the only byproduct (Scheme 43).

When a benzene solution containing 10 mmol of pyrrolidine, 10 mmol of ethyl acetate and 0.01 mmol of complex 1 was refluxed under Argon atmosphere, quantitative conversion of pyrrolidine was observed by GC after 28 hrs, to yield 98% of N-acetyl pyrrolidine after column purification (Table 29, entry 1). The N-acetyl pyrrolidine was characterized by NMR and GC-MS. Similar results were obtained in toluene. Reaction of ethyl acetate with morpholine in benzene under reflux resulted after 36 hrs in 79% conversion with the isolation of the corresponding amide in 77% yield (Table 29, entry 2). Refluxing of 1-methyl piperazine, ethyl acetate and benzene in the presence of complex 1 provides the corresponding amide in 56% yield with the conversion of the ester being 59% (Table 29, entry 3).

Various esters and amines reacted similarly. Refluxing a toluene solution containing butyl butyrate (5 mmol), piperidine (10 mmol) and 0.1 mol % of the PNN complex 1 under argon atmosphere for 19 hrs resulted in 100% conversion of piperidine as observed by GC analysis, with the exclusive formation of the 1-(piperidin-1-yl)butan-1-one in 94% yield after isolation from alumina column chromatography (Table 29, entry 4). The product was completely characterized by NMR spectroscopy. Unlike the traditional methods, this reaction does not form any alcohol as by-product, resulting in the irreversible, unique incorporation of both the acyl and alkoxo parts of the starting ester into the product amide. Significantly the TON of ester-amide exchange reaction was high (1000). Similarly, refluxing the toluene solution containing butyl butyrate, morpholine or N-methyl piperazine in the presence of complex 1 resulted in 100% conversion of the amine with the isolation of the amides in 95 and 94% yields, respectively. Refluxing of excess of butyl butyrate and piperazine in toluene led to bis-acylation of the piperazine, providing the corresponding amide in 61% yield.

To explore the synthetic utility of this reaction, pentyl pentanoate was reacted with various amines. The reaction of pentyl pentanoate with piperidine gave 100% conversion with the isolation of the amide in 96% yield. Morpholine and N-methyl piperazine furnished the respective amide in 96 and 94% isolated yield.

Next, reactions were studied with primary amines. The reaction of ethyl butyrate and hexyl amine in the presence of 0.1 mol % of 1 in refluxing toluene led to 100% conversion of the hexyl amine with the isolation of 97% of the corresponding amide as the only product. Similarly, reaction of pentyl pentanoate and 4-methylbenzyl amine in refluxing toluene resulted in 100% conversion with isolation of corresponding amide in 98% yield. These reactions did not lead any alcohol as waste product.

The reactions were also studied in absence of solvent. Thus, heating pentylpentanoate, piperidine and complex 1 at 135° C. resulted in 52% conversion.

TABLE 29
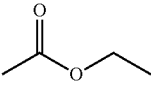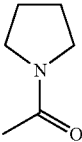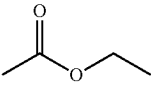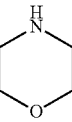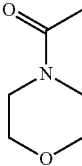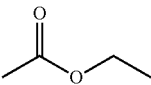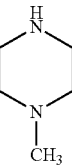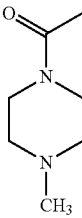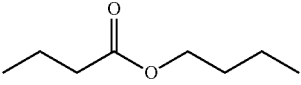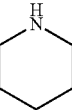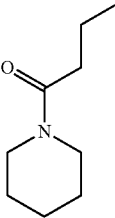
Amination of esters catalyzed by the ruthenium complex 1[a]

Entry	Ester	Amine	Time (hrs)	Conv. of amine	Isolated Yield (%)
1			26	100	99
2			36	79	77
3			24	59	56
4			19	100	94

TABLE 29-continued
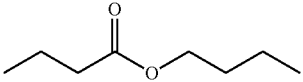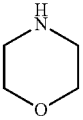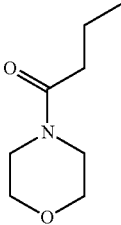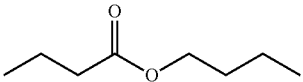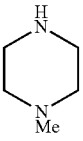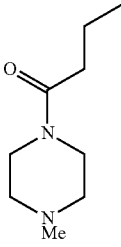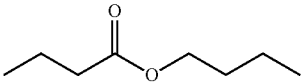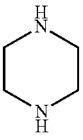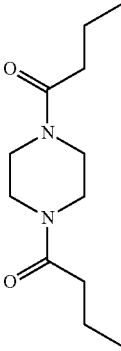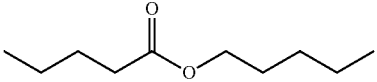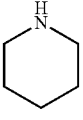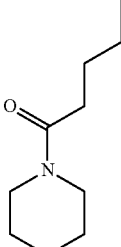
| | | | | Conv. | |
| En- | | | Time | of | |
try	Ester	Amine	(hrs)	amine	Isolated Yield (%)
5			21	100	
					95
6			24	100	
					94
6			36	100	
					61
7			19	100	
					96
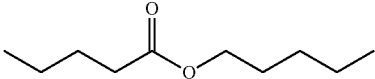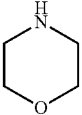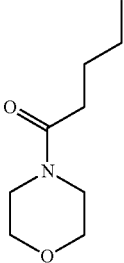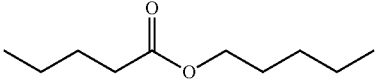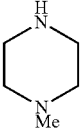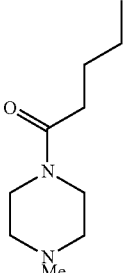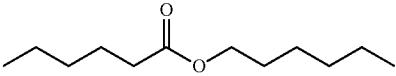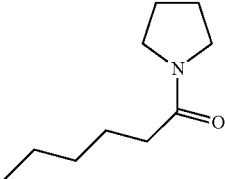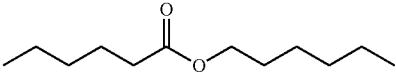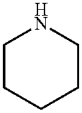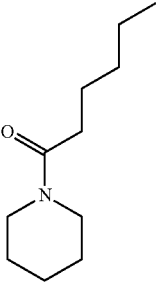
Amination of esters catalyzed by the ruthenium complex 1[a]

TABLE 29-continued

				Conv. of amine	
En-try	Ester	Amine	Time (hrs)		Isolated Yield (%)
8			26	100	92
9			24	100	94
10			18	100	97
11			26	100	94

Amination of esters catalyzed by the ruthenium complex 1[a]

TABLE 29-continued

Amination of esters catalyzed by the ruthenium complex 1[a]

En-try	Ester	Amine	Time (hrs)	Conv. of amine	Isolated Yield (%)
12			18	100	93
13			24	100	97
14			18	100	98

[a]Complex 1 (0.01 mmol), ester (5 mmol), amine (10 mmol) and toluene/benzene (3 ml) were refluxed at an oil bath temperature of 135° C. in a Schlenk tube. Conversion of amine was analyzed by GC using m-xylene as internal standard.

In summary, acylation of amines using esters as the acylating partner is efficiently catalyzed by complex 1 under neutral conditions. The use of symmetrical esters results in the incorporation of both the acyl and alkoxo parts of the substrate ester into the product amide with liberation of H_2. This offers an environmentally benign, atom economical method for amide synthesis from esters without any waste generation. This catalytic cycle produces a high turnover number (1000) and both primary and secondary amines can be used.

Example 13

Ruthenium-Pincer Catalyzed Acylation of Alcohols Using Esters with Liberation of H_2 Under Neutral Conditions

The acylation of esters with secondary alcohols can be carried out selectively to give the mixed ester using the PNN catalyst 1. The reaction is general, efficient, and environmentally benign. It proceeds under neutral conditions without acids or bases, activators, or molecular sieves. Uniquely, when a symmetrical ester (such as ethyl acetate) is reacted with a secondary alcohol, the only co-product is molecular hydrogen, unlike the generally employed transesterification reaction which gives an alcohol co-product (or its derivative) (Scheme 44).

Scheme 44. Acylation of alcohols using esters.
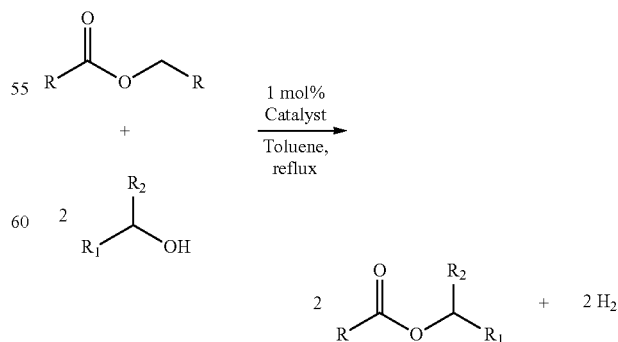
When a benzene solution containing 15 mmols of cyclohexanol, 5 mmols of ethyl acetate and 0.05 mmols of complex

1 was refluxed under argon atmosphere, GC analysis after 28 hrs showed that all of the ethyl acetate disappeared and cyclohexyl acetate was formed as a single product (Table 30, entry 1). ^{1}H NMR and GC-MS of the isolated product were identical to cyclohexyl acetate prepared by refluxing neat acetic anhydride with cyclohexanol.

Likewise, refluxing a toluene solution containing one equivalent of hexyl hexanoate, 2 equivalents of cyclohexanol and 1 mol % of the PNN complex 1 under argon atmosphere for 20 h resulted in 84% conversion of hexyl hexanoate as determined by GC analysis, with the exclusive formation of the ester cyclohexyl hexanoate in 83% yield (Table 30, entry 2). Notably, unlike the traditional transesterification methods, this reaction does not form an alcohol product; rather, an irreversible incorporation of both the acyl and alkoxo parts of the starting ester into the product ester takes place. While 2 equivalents of the alcohol with respect to the ester are sufficient, somewhat higher yields are obtained when 3 equivalents of alcohol were used. Thus, reaction of 3 equivalents of cyclohexanol with hexyl hexanoate resulted after 26 h in 96% conversion with 95% yield of cyclohexyl hexanoate, as observed by GC, and confirmed by GC-MS by comparison with an authentic sample (Table 30, entry 3). The pure product was isolated by evaporation of the solvent followed by passing through a basic alumina plug and analysis by NMR and GC-MS. Use of the PNP complexes 2 or 3 resulted after 20 h in 58% or 17% yield of cyclohexyl hexanoate, respectively. Studying the scope of this new reaction with regard to the secondary alcohol, reaction of hexyl hexanoate with cyclopentanol in the presence of 1 mol % 1 was carried out. After 26 h reflux in toluene, cyclopentyl hexanoate (70% yield) was formed, with 71% conversion of hexyl hexanoate (Table 30, entry 4). Similarly, upon reaction of hexyl hexanoate with excess of 1-phenylethanol, 50% conversion of hexyl hexanoate with the formation of 49% of the acylated product was observed (Table 30, entry 5). The lower conversion of the ester is a result of facile dehydrogenation of 1-phenylethanol to acetophenone (49%). Because of the expected easy dehydrogenation of the isopropyl alcohol to acetone, transesterification with this alcohol was performed in a closed vessel, to retard this dehydrogenation process. Thus, heating hexyl hexanoate with excess of isopropyl alcohol resulted after 19 h in 83% conversion of hexyl hexanoate

with the formation of isopropyl hexanoate in 67% yield (entry 6). The reaction of hexyl hexanoate and 3-pentanol led to 91% conversion of the ester with formation of 3-pentyl hexanoate in 90% yield after 26 h reflux (entry 7).

Exploring further the scope with regard to the ester substrate, pentyl pentanoate was reacted with cyclohexanol, resulting in 93% conversion with the formation of 93% cyclohexyl pentanoate (entry 8). Like in the case of hexyl hexanoate, the presumably formed pentanol intermediate is converted into pentyl pentanoate with the liberation of H$_2$. Similarly, treatment of pentyl pentanoate with cyclopentanol, 1-phenylethanol and 3-pentanol, furnished 87, 51, 91% conversion of pentyl pentanoate, respectively, with the predominant formation of the corresponding cross-ester as the product in 85, 49, 90% yields, respectively (entries 9-11).

Next we studied the reaction of butyl butyrate with various secondary alcohols. Reaction of 5 mmol of butyl butyrate with 15 mmol of cyclohexanol led to 93% conversion of the ester with the formation of 92% of cyclohexyl butyrate after 34 h (entry 12). Upon refluxing of butyl butyrate with cyclopentanol, after 28 hrs 75% conversion of the ester, with formation of 74% cyclopentyl butyrate were observed (entry 13). In a similar reaction with 1-phenylethanol or 3-pentanol, 41 and 77% conversion, respectively, into the product was noted by GC analysis after 36 h (entries 14 and 15).

These reactions were also studied with unsymmetrical esters. The reaction of ethyl butyrate with 3-pentanol in the presence of 1 mol % of 1 under refluxing toluene led to 75% conversion of ethyl butyrate with the formation of 73% of 3-pentyl butyrate as the exclusive product (entry 16). Traces of 3-pentyl acetate, resulting from reaction with the formed ethanol, were also observed. The remaining ethanol probably evaporated from the reaction mixture under the reflux conditions. Similarly, the reaction of methyl hexanoate with cyclohexanol results in 42% conversion after 17 h with the formation of 42% of cyclohexyl hexanoate (entry 17).

Since the dehydrogenation of the secondary alcohol to ketone is slower than the dehydrogenative coupling of the primary alcohol to ester, most of the secondary alcohol reacts with the ester, although some ketone resulting from excess alcohol was observed. The slow reaction of the secondary alcohol with PNN complex may be due to the steric hindrance.

TABLE 30
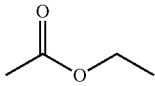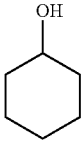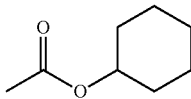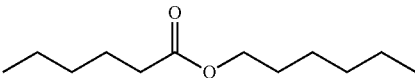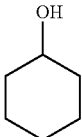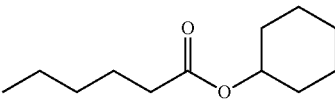
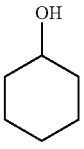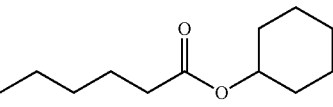|						
En-try	Ester		alcohol	Time (hrs)	Conv. of ester %	Yield %
1$^{b)}$				28	100	
2$^{c)}$				20	84	
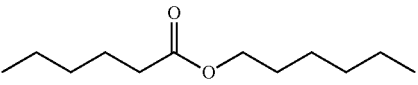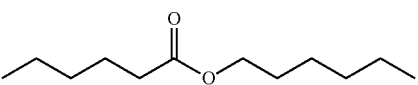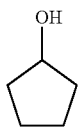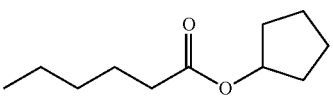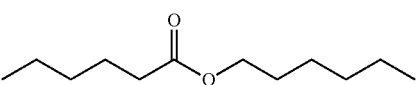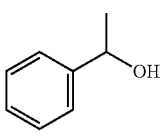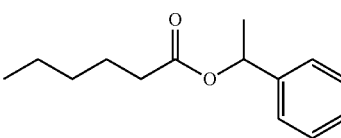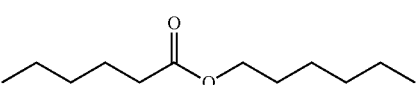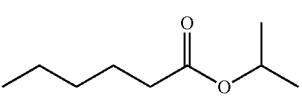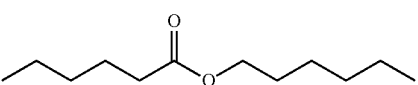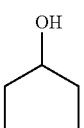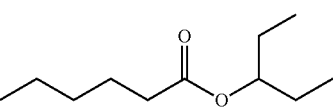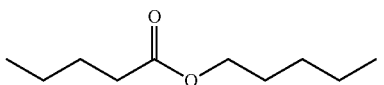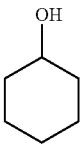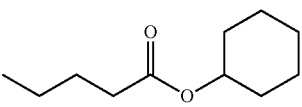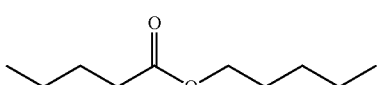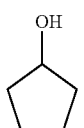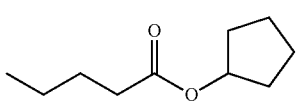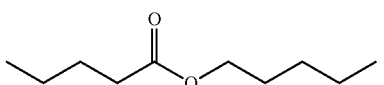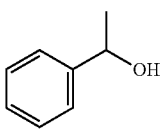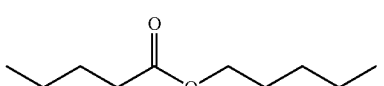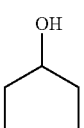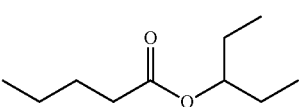
Acylation of alcohols catalyzed by the ruthenium complex 1$^{a)}$

TABLE 30-continued
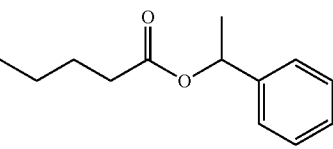
Acylation of alcohols catalyzed by the ruthenium complex 1[a)]

En-try	Ester	alcohol	Time (hrs)	Conv. of ester %	Yield %
3			26	96 (cat 1) 58 (cat. 2) 17 (cat. 3)	95 (cat 1)
4			26	71	70
5			36	50	49
6[d)]			19	83	67
7			26	91	90
8			36	93	93
9			36	87	85
10			18	51	49
11			26	91	90

TABLE 30-continued

Acylation of alcohols catalyzed by the ruthenium complex 1[a]

En-try	Ester	alcohol	Time (hrs)	Conv. of ester %	Yield %
12			34	93	92
13			28	75	74
14			36	41	39
15			18	77	76
16[e]			20	75	73
17			17	42	42

[a]Complex 1 (0.05 mmol), ester (5 mmol), alcohol (15 mmol) and toluene (3 ml) were refluxed/heated at an oil bath temperature of 135° C. under argon. Conversion of ester and yield of product were analyzed by GC using m-xylene or benzene as internal standards. A small amount of the secondary alcohol was converted into the corresponding ketone.
[b]Benzene was used as solvent. Efficient cooling of the reflux condenser is required to avoid losses of ethyl formate.
[c]1 (0.05 mmol), hexyl hexanoate (5 mmol), cyclohexanol (10 mmol) and toluene (3 ml) were used.
[d]a closed system and 3 ml of 2-propanol were used. An equivalent amount of 1-hexanol (67%) was also detected.
[e]m-xylene was used as solvent and benzene as internal standard.

Experimental Section

General Procedure for the Catalytic Acylation of Alcohols:

Complex 1 (0.05 mmol), ester (5 mmol), alcohol (15 mmol) and toluene (3 mL) were added to Schlenk flask under an atmosphere of nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for the specified time (Table 30). In the case of isopropanol, the reactions were performed in a closed system at 135° C. The reaction products were analyzed by GC-MS. After cooling to room tempera-ture, m-xylene (1 mmol) or benzene (1 mmol) were added as internal standards to the reaction mixture and the products were quantitatively analyzed by GC using a Carboxen 1000 column on a HP 690 series GC system or HP-5 cross linked 5% PH ME Siloxane column (30 m×0.32 mm×0.25 µm film thickness) on a HP 6890 series GC system. In the reaction of cyclohexanol and esters, evaporation of the solvent, followed by purification over basic alumina column chromatography afforded the pure transesters. ^{1}H NMR of the products iso-lated from the catalysis was identical with the literature.
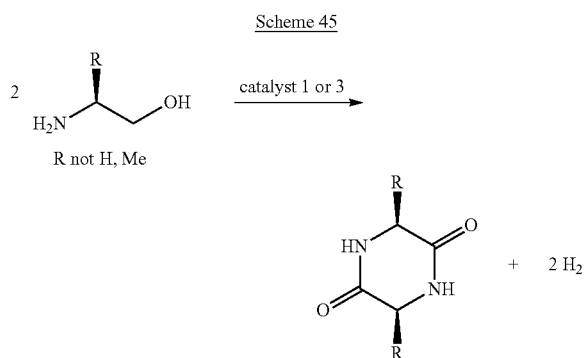
Example 14

Synthesis of Cyclic Dipeptides and Pyrazines from β-Aminoalcohols

A. Formation of Cyclic Dipeptides

Dehydrogenative coupling of β-aminoalcohols can lead to cyclic dipeptide formation (Scheme 45), except in case of R═H, Me (in which case linear polypeptides are the main products; in case of R═Me, a small amount of cyclic dipeptide is also formed).

Scheme 45

Refluxing a dioxane solution of (S)-2-amino-4-methylpentan-1-ol with complex 1 (1 mol %) led to 64% isolated yield of the cyclic dipeptide, 3,6-diisobutylpiperazine-2,5-dione 7b after workup (Table 31, entry 1). The product structure was confirmed by MS, NMR spectroscopies.

Upon refluxing a dioxane solution containing 2 mmol of (2S,3S)-2-amino-3-methylpentan-1-ol and 0.02 mmol of catalyst 1 for 19 hrs and cooling the reaction mixture, the solid product precipitated and was filtered off and dried under vacuum to give pure 3-(sec-butyl)-6-(sec-butyl)piperazine-2, 5-dione 7c in 72% yield (Table 31, entry 2). The structure was confirmed by NMR and MS spectroscopies. Under the same conditions, cyclic peptidation of (S)-2-amino-3-methylbutan-1-ol led to 3,6-diisopropylpiperazine-2,5-dione 7d as an insoluble solid which separated from the reaction mixture and was isolated by filtration and dried under vacuum to give 78% of (3S,6S)-3,6-diisopropylpiperazine-2,5-dione 7d (Table 31, entry 3). The optical rotation of the pure product)(−52° was essentially the same as reported in the literature)(−54°). Thus, under these experimental condition, no racemization took place.

The reaction of (S)-2-amino-3-phenylpropan-1-ol and 1 in refluxing dioxane led to 90% conversion with the isolation of the corresponding 3,6-dibenzylpiperazine-2,5-dione 7e in 72% yield (Table 31, entry 4). Reaction of 2-amino-2-methylpropan-1-ol under the same conditions yielded 100% conversion with isolation of the corresponding cyclic dipeptide 3,3,6,6-tetramethylpiperazine-2,5-dione 7f in 92% yield (Table 31, entry 5).

Tricyclic ring systems represent an important structural motif in many naturally existing alkaloids. Refluxing a dioxane solution of (S)-pyrrolidin-2-yl-methanol in the presence of catalyst 1 followed by solvent evaporation, hexane addition to the crude solid, and its isolation by filtration and washing with hexane led to octahydrodipyrrolo[1,2-a:1',2'-d] pyrazine-5,10-dione 7 g in 99% isolated yield (Table 31, entry 6).
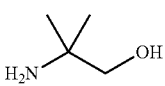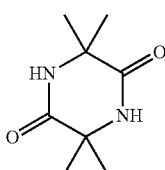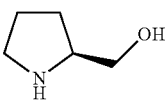
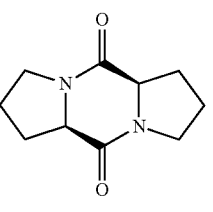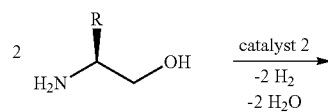TABLE 31

		Synthesis of cyclic dipeptides from β-aminoalcohols catalyzed by complex 1.		
Entry	Catalyst	Aminoalcohol	cyclic dipeptide	Isolated Yields (%)
1	1		7b	64
2	1		7c	72
3	3		7d	87
4	3		7e	82

TABLE 31-continued

Synthesis of cyclic dipeptides from β-
aminoalcohols catalyzed by complex 1.

En-try	Cata-lyst	Aminoalcohol	cyclic dipeptide	Iso-lated Yields (%)
5	1		7f	92
6	1		7g	99

[a] Complex 1 or 3 (0.02 mmol), aminoalcohol (2 mmol) and dioxane (2 ml) were refluxed under argon (oil bath temperature of 135° C.) for 19 h.

B. Formation of Pyrazines

Pyrazines are biologically important organic compounds and their synthesis is of industrial significance. When the RuPNP complex 2 was used as catalyst, pyrazine derivatives were obtained from β-amino alcohols (Scheme 46). Thus, a toluene solution of isoleucinol with complex 2 (1 mol %) was vigorously refluxed under argon for 24 hrs resulting in complete conversion of isoleucinol. The solvent was evaporated under vacuum and the residue was subjected to silica-gel column chromatography to afford 2,6-diiso-butyl pyrazine 8a in 53% yield (Table 32, Entry 1). ^{1}H NMR exhibits the characteristic aromatic CH at 8.27 ppm and GC-MS confirms the respective molecular weight. The same reaction was also conducted by reflux under air using complex 2, resulting in 48% isolated yield of 8a. The similarity in yields of 8a under argon and under air indicates that air does not play a role as oxidant in the dehydrogenation of the presumed intermediate 1,4-dihydropyrazine to form the pyrazine. Significantly, no cyclic dipeptide was obtained under these conditions. Similar results were obtained with other aminoalcohols. Thus, toluene solutions of (S)-2-amino-3-methylbutan-1-ol, (S)-2-amino-4-methylpentan-1-ol, and (S)-2-amino-2-phenylethanol, were vigorously refluxed (bath temperature 165° C.) for 24 hrs while monitoring reaction progress by GC-MS. After complete disappearance of the amino alcohol, the crude product was purified by column chromatography to get the corresponding pyrazine products 8b-d (Table 32).
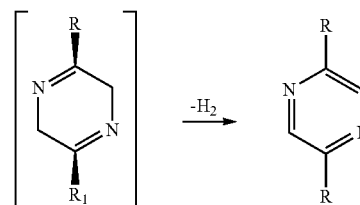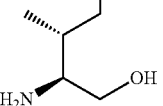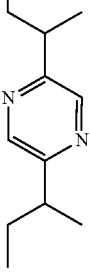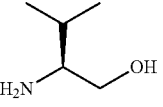
Scheme 46
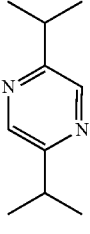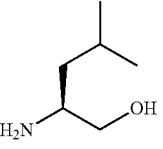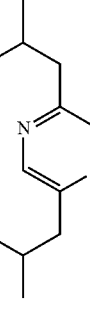
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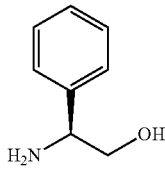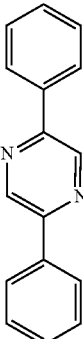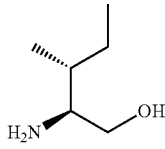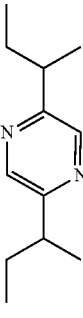

TABLE 32

Synthesis of pyrazines from β-aminoalcohols
catalyzed by the ruthenium PNP complex 2.(a)

Entry	β-Aminoalcohol	Pyrazine	Isolated Yields (%)
1		8a	53
2		8b	35
3[(b)]		8c	38

TABLE 32-continued

Synthesis of pyrazines from β-aminoalcohols
catalyzed by the ruthenium PNP complex 2.(a)

Entry	β-Aminoalcohol	Pyrazine	Isolated Yields (%)
4		 8d	45
5[c]		 8a	48

(a)Complex 2 (0.02 mmol), aminoalcohol (2 mmol) and toluene (2 ml) were vigorously refluxed (oil bath temperature at 165° C. for 24 h).

[b]Heated in absence of solvent (oil bath temperature at 165° C.).

[c]Reaction performed under air.

## General Procedure for the Synthesis of Cyclic Dipeptides from β-Aminoalcohols:

Complex 1 (0.02 mmol), aminoalcohol (2 mmol) and dioxane (2 mL) were added to Schlenk flask under an atmosphere of nitrogen in a glovebox. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 19 hrs. The reaction products were analyzed by GC-MS on Agilent 7820A GC coupled with 5975 MSD system. The reaction mixture was cooled; the solid obtained was filtered off, washed with hexane and dried to give the pure cyclic dipeptide.

General Procedure for the Synthesis of Pyrazines from β-Aminoalcohols:

Complex 2 (0.02 mmol), aminoalcohol (2 mmol) and toluene (2 mL) were added to Schlenk flask under an atmosphere of nitrogen in a glovebox. The flask was equipped with a condenser and the solution was refluxed with stirring under argon in an open system for the 24 hrs. The reaction products were analyzed by GC-MS on Agilent 7820A GC coupled with 5975 MSD system. The solvent was evaporated from the reaction mixture and the crude product was subjected to

silica-gel column chromatography using EtOAc:hexane to afford the pyrazine derivatives.

Characterization Data of Cyclic Dipeptides
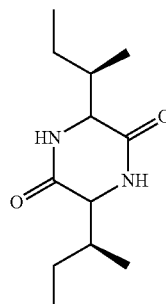
(3S,6S)-3,6-diisobutylpiperazine-2,5-dione
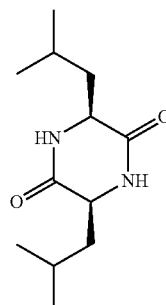
mp: 270-272° C.

^{1}H NMR (300 MHz, CD$_3$COOD): 0.84 (broad s, 12H, CH$_3$), 1.7 (broad s, 6H, CH$_2$, CH), 4.23 (broad s, 2H, NCH).

^{13}C{^{1}H}NMR (300 MHz, CDCl$_3$): 21.3 (CH$_3$), 21.6 (CH$_3$), 23.7 (CH$_3$), 23.8 (CH$_3$), 26.0 (CH), 26.2 (CH), 43.7 (CH$_2$), 46.4 (CH$_2$), 55.4 (NCH), 55.8 (NCH), 174.9 (C=O), 175.0 (C=O).

MS (ES$^+$, CH$_2$Cl$_2$+TFA): 227 (60%, M+H$^+$), 249 (100%, M+Na), 475 (70%, 2M+Na).
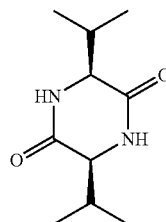
3-((R)-sec-butyl)-6-((S)-sec-butyl)piperazine-2,5-dione

mp: 276-280° C. (decompose)

^{1}H NMR (300 MHz, CDCl$_3$): 0.86-1.02 (m, 12H, CH$_3$), 1.19-1.47 (m, 4H, CH$_2$), 2.10-2.26 (m, 2H, CH$_2$), 3.91-4.07 (m, 2H, NCH), 6.11-6.31 (m, 2H, NH).

MS (ES$^+$, CH$_2$Cl$_2$+TFA): 227 (40%, M+H), 244 (100%), 249 (40%, M+Na), 467 (80%), 475 (5%, 2M+Na).

(3S,6S)-3,6-diisopropylpiperazine-2,5-dione

mp: 290-294° C. (decompose)

^{1}H NMR (300 MHz, CDCl$_3$ and CD$_3$COOD): 0.91 (d, J=6.6 Hz, 6H, CH$_3$), 1.01 (d, J=6.6 Hz, 6H, CH$_3$), 2.44-2.53 (m, 2H, CH), 4.11 (m, 2H, NCH).
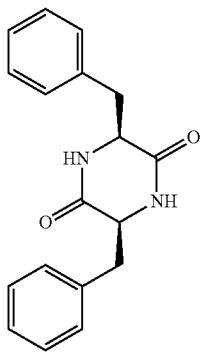
137

^{13}C{^{1}H}NMR (300 MHz, CDCl$_3$): 15.7 (CH$_3$), 18.2 (CH$_3$), 32.3 (CH), 59.8 (NCH), 171.2 (C=O).

MS (ES$^+$, CH$_2$Cl$_2$+TFA): 199 (100%, M+H$^+$), 221 (60%, M+Na), 419 (15%, 2M+Na).

[α]=−52° (c=0.01, AcOH)

(3S,6S)-3,6-dibenzylpiperazine-2,5-dione

mp: 299-302° C. (decompose)

^{1}H NMR (300 MHz, CDCl$_3$ and CD$_3$COOD): 2.15-2.22 (m, 2H, CH$_2$), 2.95-3.01 (m, 2H, CH$_2$), 4.39-4.43 (m, 2H, NCH), 7.03 (d, J=6.9 Hz, 4H, =CH), 7.31-7.39 (m, 6H, =CH).

^{13}C{^{1}H}NMR (300 MHz, CD$_3$COOD): 39.6 (CH$_2$), 56.2 (NCH), 128.4 (=CH), 129.4 (=CH), 129.9 (=CH), 133.5 (quat-C), 169.9, 173.0 (C=O).

MS (ES$^+$, CH$_2$Cl$_2$+TFA): 295 (80%, M+H), 317 (100%, M+Na), 611 (60%, 2M+Na).

3,3,6,6-tetramethylpiperazine-2,5-dione
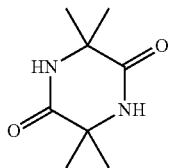
^{1}H NMR (300 MHz, DMSO-d$_6$): 1.30 (s, 12H, CH$_3$), 8.09 (s, 2H, NH).

^{13}C{^{1}H}NMR (300 MHz, DMSO-d$_6$): 28.6 (CH$_3$), 55.7 (quat-C), 170.2 (C=O).

MS (ES$^+$): 170 (100%, M$^+$), 192 (30%), 200 (25%).

(5aS,10aS)-octahydrodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10-dione
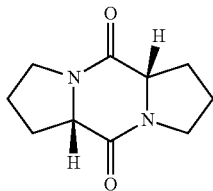
mp: 146-148° C.

^{1}H NMR (300 MHz, CDCl$_3$): 1.88-2.33 (m, 8H, CH$_2$), 3.49-3.54 (m, 4H, NCH$_2$), 4.16 (t, 2H, NCH).

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^{13}C{^{1}H}NMR (300 MHz, CDCl$_3$): 23.3 (CH$_2$), 27.6 (CH$_2$), 45.1 (NCH$_2$), 60.5 (NCH), 166.3 (C=O).

MS (ES): 194 (70%, M), 216 (100%, M+Na-1), 217 (10%, M+Na).

Characterization Data of Pyrazines

2,5-di-sec-hutylpyrazine
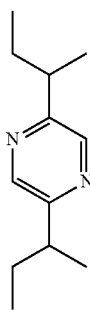
^{1}H NMR (300 MHz, CDCl$_3$): 0.77 (t, 6H, CH$_3$, J=7.2 Hz), 1.22 (d, 6H, CH$_3$, J=6.9 Hz), 1.52-1.74 (m, 4H, CH$_2$), 2.68-2.76 (m, 2H, CH), 8.27 (s, 2H, =CH).

^{13}C{^{1}H}NMR (300 MHz, CDCl$_3$): 11.6 (CH$_3$), 19.6 (CH$_3$), 29.3 (CH$_2$), 40.2 (CH), 142.4 (=CH), 158.1 (quat-C).

2,5-diisopropylpyrazine
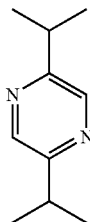
^{1}H NMR (300 MHz, CDCl$_3$): 1.23 (d, 12H, CH$_3$, J=7.2 Hz), 2.95-3.04 (m, 2H, CH), 8.30 (s, 2H, =CH).

^{13}C{^{1}H}NMR (300 MHz, CDCl$_3$): 21.8 (CH$_3$), 33.1 (CH), 141.4 (=CH), 158.9 (quat-C).

2,5-diisobutylpyrazine
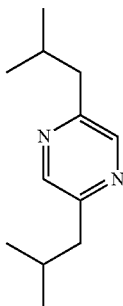
^{1}H NMR (300 MHz, CDCl$_3$): 0.94 (d, 12H, CH$_3$, J=6.6 Hz), 2.04-2.13 (m, 2H, CH), 2.63 (d, 4H, CH$_2$, J=7.2 Hz), 8.32 (s, J=6.9 Hz, 2H, =CH).

$^{13}C\{^1H\}$NMR (300 MHz, CDCl$_3$): 21.9 (CH$_3$), 28.6 (CH), 43.6 (CH$_2$), 143.5 (=CH), 153.4 (quat-C).

2,5-diphenylpyrazine
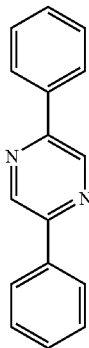
^{1}H NMR (300 MHz, CDCl$_3$): 7.48-7.57 (m, 6H, =CH$_3$), 8.07-8.10 (m, 4H, =CH), 9.09 (s, 2H, =CH).

$^{13}C\{^1H\}$NMR (300 MHz, CDCl$_3$): 126.8 (=CH), 129.1 (=CH), 129.7 (=CH), 136.3 (quat-C), 141.2 (=CH), 150.6 (quat-C).

While certain embodiments of the invention have been illustrated and described, it will be clear that the invention is not limited to the embodiments described herein. Numerous modifications, changes, variations, substitutions and equivalents will be apparent to those skilled in the art without departing from the spirit and scope of the present invention as described by the claims, which follow.

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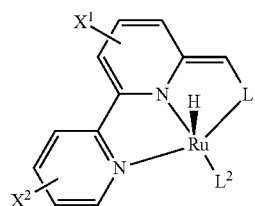
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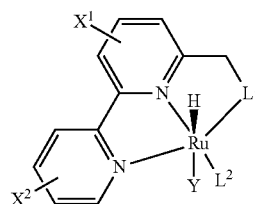
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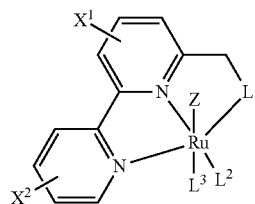(28) R. Holm, *Inorg. Synth.* 1970, 12, 238-240.

What is claimed is:

1. A Ruthenium complex represented by the structure of any of formulae B1, B2 or A3:
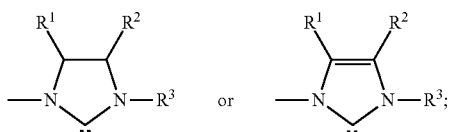

B1

B2

B3

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl contain-

ing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:

L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)$ (OR^c), NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;

L^3 is absent or is L^2;

Y and Z are each independently H or an anionic ligand selected from the group consisting of H, halogen, OCOR, $OCOCF_3$, OSO_2R, OSO_2CF_3, CN, OR, $N(R)_2$ and RS;

R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and

anion represents a group bearing a single negative charge; or

a borane derivative of said catalyst.

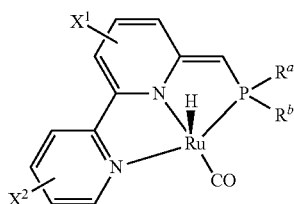**2**. The complex according to claim **1**,

wherein X^1 and X^2 are each absent, and the bipyridine moiety is unsubstituted; or

wherein L^1 is phosphine (PR^aR^b); or

wherein L^2 is CO; or

wherein Z and Y are H or halogen.

3. The Ruthenium complex according to claim **1**, wherein the catalyst is represented by formula C1:

wherein each of X^1, X^2 R^a and R^b are as defined in claim **1**.

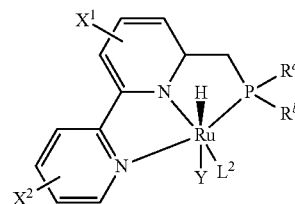**4**. The Ruthenium complex according to claim **1**, wherein the catalyst is represented by formula C2:

wherein each of X^1, X^2, Y, R^a and R^b are as defined in claim **1**.

5. The Ruthenium complex according to claim **4**,

wherein Y is halogen; or
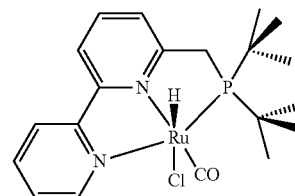
wherein L^2 is CO; or

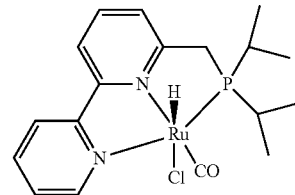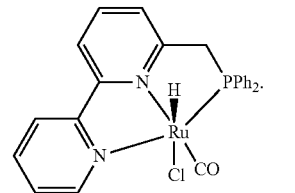wherein the Ruthenium complex is represented by the structure of formulae 4, 7 or 9:
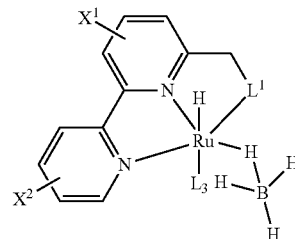

6. A borane derivative of the complex of formula A1 according to claim **1**, wherein the borane derivative is represented by the structure of formula D, E or 8':
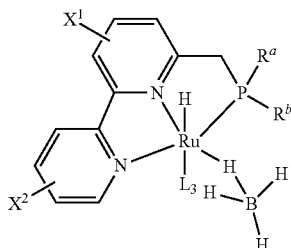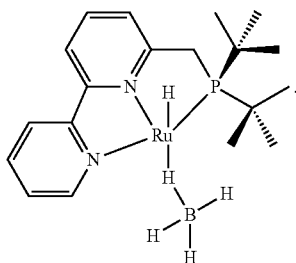

wherein L^1, X^1 and X^2 are as defined in claim **1**;

E

wherein each of X^1, X^2, R^a and R^b is as defined in claim **1**;

8'

7. A process for hydrogenating an amide to an alcohol and an amine, comprising the step of reacting the amide with molecular hydrogen (H_2) in the presence of the Ruthenium complex according to claim **1**

wherein the process comprises the step of hydrogenating an amide represented by the formula $R^4C(=O)$—N—$R^5R^{5'}$ to an alcohol of formula R^4CH_2OH and amine of formula $R^5R^{5'}NH$:
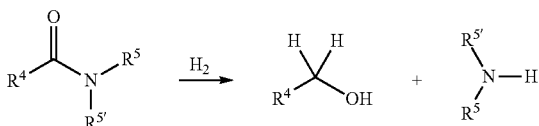
wherein R^4, R^5 and $R^{5'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

8. A process for hydrogenating an ester, organic carbonate, carbamate or urea derivative, comprising the step of reacting the ester, organic carbonate, carbamate or urea derivative with molecular hydrogen (H2) in the presence of the Ruthenium complex according to claim **1**, thereby hydrogenating the ester, organic carbonate, carbamate or urea derivative and generating at least one alcohol, amine or combination thereof.

9. The process of claim **8**, comprising the step of hydrogenating an ester represented by the formula $R^6C(=O)$—OR^7 to the corresponding alcohol or alcohols:
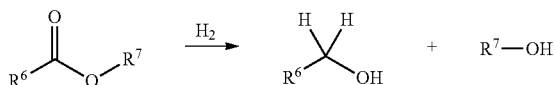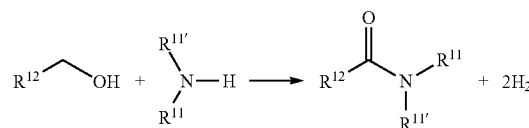

wherein
R^6 is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and

R^7 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.
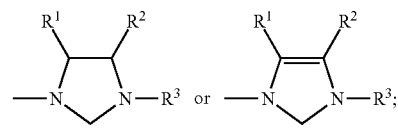
10. A process for preparing an amide, comprising the step of reacting a primary or secondary amine with a primary alcohol in the presence of the Ruthenium complex according to claim **1**, thereby generating the amide and molecular hydrogen,

wherein said process comprises reacting an amine represented by formula $R^{11}R^{11'}NH$ with an alcohol represented by the formula $R^{12}CH_2OH$ to generate an amide represented by the structure R^{12}—$C(=O)$—$NR^{11}R^{11'}$:

wherein R^{10}, R^{11} and R^{12} are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

11. A process for preparing a pyrazine, comprising the step of reacting a beta-amino alcohol with a Ruthenium complex according to claim **1**, wherein L^1 is selected from a phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:

wherein R^1, R^2, R^3, R^a and R^b are as defined in claim **1**.

12. A process for preparing an ester by dehydrogenative coupling of primary alcohols, comprising the step of reacting a primary alcohol or a combination of primary alcohols in the presence of the Ruthenium complex according to claim **1**, thereby generating the ester and molecular hydrogen,
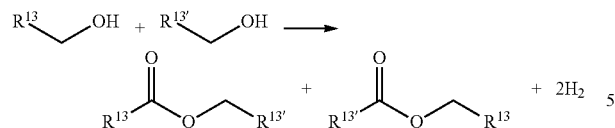
wherein the process comprises the step of converting a primary alcohol represented by formula $R^{13}CH_2OH$ to an ester by the structure R^{13}—$C(=O)$—OCH_2R^{13}:
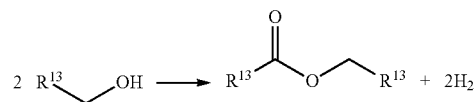
wherein R^{13} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; or

wherein the process comprises the steps of reacting a first primary alcohol represented by formula $R^{13}CH_2OH$ with a second alcohol represented by formula $R^{13'}CH_2OH$ so as to generate an ester by the structure R^{13}—$C(=O)$—$OCH_2R^{13'}$ or an ester of formula $R^{13'}$—$C(=O)$—OCH_2R^{13}
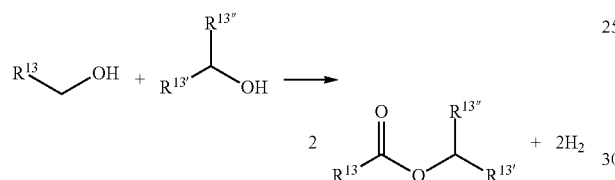
wherein R^{13} and $R^{13'}$ are the same or different from each other and are each independently selected is from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

13. A process for preparing an ester by dehydrogenative coupling of a primary alcohol and a secondary alcohol comprising the step of reacting the primary and secondary alcohol in the presence of the Ruthenium complex according to claim **1**, thereby generating the ester and molecular hydrogen,
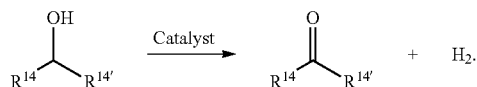
wherein the process comprises the step of reacting a primary alcohol represented by formula $R^{13}CH_2OH$ with a secondary alcohol of formula $R^{13'}R^{13''}CHOH$ so as to generate an ester by the structure R^{13}—C(=O)—OCHR$^{13'}R^{13''}$:

wherein R^{13}, $R^{13'}$ and $R^{13''}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

14. A process for preparing a ketone by dehydrogenation of a secondary alcohol, comprising the step of reacting the secondary alcohol in the presence of the Ruthenium complex according to claim **1**, thereby generating the ester and molecular hydrogen,

wherein the process comprises the step of converting a secondary alcohol represented by formula $R^{14}CH(OH)$ $R^{14'}$ to a ketone represented by the structure R^{14}—C(=O)—$R^{14'}$:
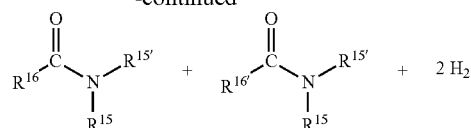

15. A process for preparing an amide, comprising the step of reacting a primary or secondary amine with an ester in the presence of the Ruthenium complex according to claim **1**, thereby generating the amide and molecular hydrogen,

wherein the process comprises the step of reacting an amine represented by formula $R^{15}R^{15'}NH$ with an ester represented by the formula R^{16}—C(=O)—OCH$_2R^{16'}$ to generate an amide represented by the structure R^{16}—C(=O)—NR$^{15}R^{15'}$:
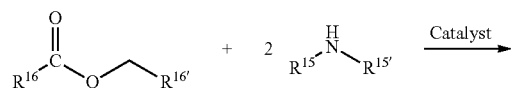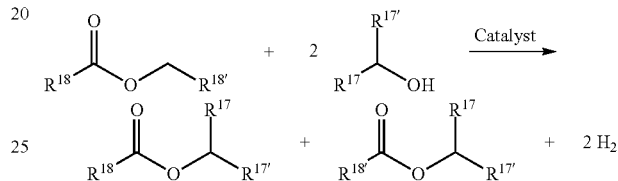
-continued

wherein R^{15}, $R^{15'}$, R^{16} and $R^{16'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

16. A process for modifying an ester by reacting a primary or secondary alcohol with an ester in the presence of the Ruthenium complex according to claim **1**, thereby generating the ester and molecular hydrogen,

wherein the process comprises the step of reacting a primary or secondary alcohol represented by formula $R^{17}R^{17'}CHOH$ with an ester by the structure R^{18}—C (=O)—OCH$_2R^{18'}$:

wherein R^{17}, $R^{17'}$, R^{18} and $R^{18'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.
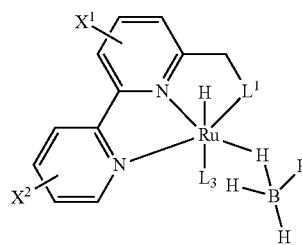
17. A process for preparing a carboxylic acid comprising the step of reacting a primary alcohol with water and a base in the presence of the Ruthenium complex according to claim **1**, thereby generating the carboxylic acid and molecular hydrogen,

wherein the process comprises the step of reacting a primary alcohol represented by formula $R^{17}CH_2OH$ with water in the presence of a base so as to generate a carboxylic acid salt represented by the structure R^{17}—C(=O)O$^-$ and, optionally, if desired, converting the carboxylic acid salt to the corresponding carboxylic acid of formula R^{17}—C(=O)OH.
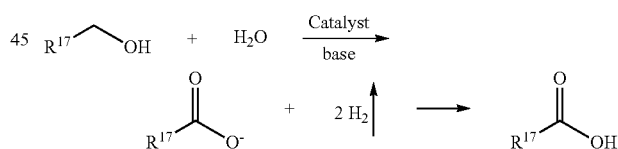
wherein R^{17} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.
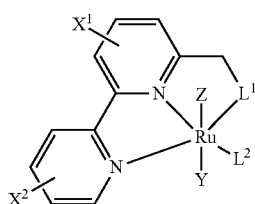
18. A process for preparing a Ruthenium complex represented by the structure of formula D according to claim **6**,
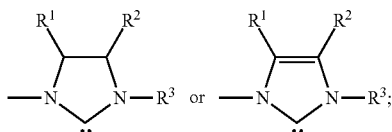
D

the process comprising the step of reacting sodium borohydride ($NaBH_4$) with a precursor of formula A2

A2

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:

L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$, NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;

L^3 is absent or is L^2;

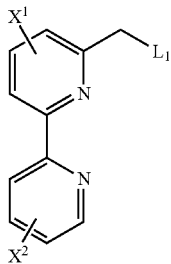Y and Z are each independently halogen, $OCOCF_3$, OSO_2R or OSO_2CF_3,

R^a, R^b and R^e are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;

R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; and
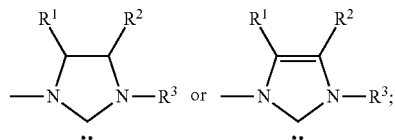
X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

19. A method for preparing the Ruthenium complex according to claim **1**, which comprises reacting a Ruthenium reagent with a compound represented by the structure of formula Z:
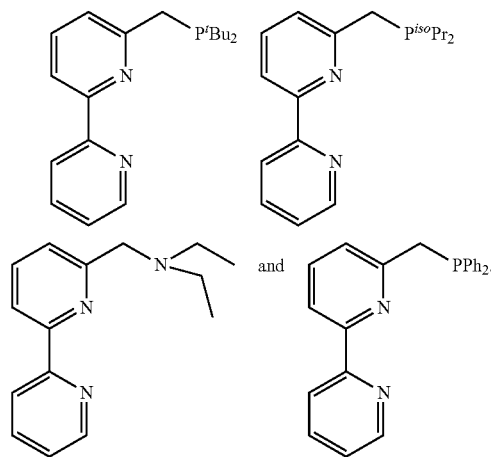

Z

wherein L^1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:
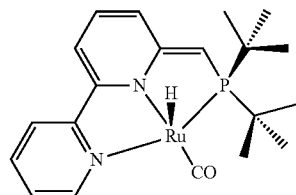

X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and

R^a and R^b are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl.

20. The method of claim **19**, wherein compound Z is selected from the group consisting of:

21. A Ruthenium complex represented by the structure of formula 3:

3

* * * * *

CERTIFICATE OF CORRECTION

PATENT NO.   : 9,045,381 B2
APPLICATION NO. : 13/880328
DATED   : June 2, 2015
INVENTOR(S)   : Milstein et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims

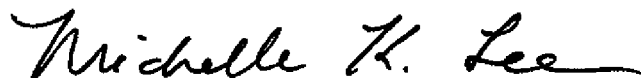<u>Column 143:</u>
Line 67, after "wherein each of X^1,", delete "X^2 R^a" and insert -- X^2, R^a --.

<u>Column 149:</u>
Line 34, after "R^a, R^b and", delete "R^e" and insert -- R^c --.

Signed and Sealed this
Twenty-ninth Day of September, 2015

Michelle K. Lee

Michelle K. Lee
Director of the United States Patent and Trademark Office